

TITLE OF THE INVENTION

O-SUPERFAMILY CONOTOXIN PEPTIDES

CROSS-REFERENCE TO RELATED APPLICATIONS

5 The present application is related to U.S. provisional patent applications Serial No. 60/173,754 filed 30 December 1999, Serial No. 60/214,263 filed 26 June 2000, Serial No. 60/219,440 filed 20 July 2000 and Serial No. 60/243,412 filed 27 October 2000.

10 This invention was made with Government support under Grant No. PO1 GM48677 awarded by the National Institute of General Medical Sciences, National Institutes of Health, Bethesda, Maryland. The United States Government has certain rights in the invention.

BACKGROUND OF THE INVENTION

15 The invention relates to relatively short peptides (termed O-Superfamily conotoxins herein), about 20-40 residues in length, which are naturally available in minute amounts in the venom of the cone snails or analogous to the naturally available peptides, and which preferably include three disulfide bonds.

20 The publications and other materials used herein to illuminate the background of the invention, and in particular, cases to provide additional details respecting the practice, are incorporated by reference, and for convenience are referenced in the following text by author and date and are listed alphabetically by author in the appended bibliography.

Conus is a genus of predatory marine gastropods (snails) which envenomate their prey. Venomous cone snails use a highly developed apparatus to deliver their cocktail of toxic conotoxins into their prey. In fish-eating species such as *Conus magus* the cone detects the presence of the fish using chemosensors in its siphon. When close enough the cone extends its proboscis and impales the fish with a hollow harpoon-like tooth containing venom. This immobilizes the fish and enables the cone snail to wind it into its mouth via the tooth held at the end of its proboscis. For general information on *Conus* and their venom see the website address <http://grimwade.biochem.unimelb.edu.au/cone/referenc.html>. Prey capture is accomplished through a sophisticated arsenal of peptides which target specific ion channel and receptor subtypes. Each *Conus* species venom appears to contain a unique set of 50-200 peptides. The composition of the venom differs greatly between species and between individual snails within each species, each optimally evolved to paralyse its prey. The active components of the venom are small peptides

toxins, typically 10-30 amino acid residues in length and are typically highly constrained peptides due to their high density of disulphide bonds.

The venoms consist of a large number of different peptide components that when separated exhibit a range of biological activities: when injected into mice they elicit a range of physiological responses from shaking to depression. The paralytic components of the venom that have been the focus of recent investigation are the α -, ω - and μ -conotoxins. All of these conotoxins act by preventing neuronal communication, but each targets a different aspect of the process to achieve this. The α -conotoxins target nicotinic ligand gated channels, the μ -conotoxins target the voltage-gated sodium channels and the ω -conotoxins target the voltage-gated calcium channels (Olivera et al., 1985; Olivera et al., 1990). For example a linkage has been established between α -, α A- & ψ -conotoxins and the nicotinic ligand-gated ion channel; ω -conotoxins and the voltage-gated calcium channel; μ -conotoxins and the voltage-gated sodium channel; δ -conotoxins and the voltage-gated sodium channel; κ -conotoxins and the voltage-gated potassium channel; conantokins and the ligand-gated glutamate (NMDA) channel. Five δ -conotoxins have been described: GmVIA (U.S. Patent No. 5,719,264); PVIA (U.S. Patent No. 5,739,276); TxVIA (Hillyard et al., 1989; Fainzilber et al., 1991); TxVIB (Fainzilber et al., 1991); NgVIA (Fainzilber et al., 1995); and TxIIA (Nakamura et al., 1996). For a partial list of *Conus* peptides and their amino acid sequences see the website address <http://pir.georgetown.edu>.

However, the structure and function of only a small minority of these peptides have been determined to date. For peptides where function has been determined, three classes of targets have been elucidated: voltage-gated ion channels; ligand-gated ion channels, and G-protein-linked receptors.

Conus peptides which target voltage-gated ion channels include those that delay the inactivation of sodium channels, as well as blockers specific for sodium channels, calcium channels and potassium channels. Peptides that target ligand-gated ion channels include antagonists of NMDA and serotonin receptors, as well as competitive and noncompetitive nicotinic receptor antagonists. Peptides which act on G-protein receptors include neurotensin and vasopressin receptor agonists. The unprecedented pharmaceutical selectivity of conotoxins is at least in part defined by a specific disulfide bond frameworks combined with hypervariable amino acids within disulfide loops (for a review see McIntosh et al., 1998).

Potassium channels comprise a large and diverse group of proteins that, through maintenance of the cellular membrane potential, are fundamental in normal biological function.

These channels are vital in controlling the resting membrane potential in excitable cells and can be broadly sub-divided into three classes: voltage-gated K⁺ channels, Ca²⁺ activated K⁺ channels and ATP-sensitive K⁺ channels. Many disorders are associated with abnormal flow of potassium ions through these channels. The identification of agents which would regulate the flow of potassium ions through each of these channel types would be useful in treating disorders associated with such abnormal flow.

It is desired to identify additional conotoxin peptides having activities of the above conopeptides, as well as conotoxin peptides having additional activities.

10 SUMMARY OF THE INVENTION

The invention relates to relatively short peptides (termed O-Superfamily conotoxins herein), about 20-40 residues in length, which are naturally available in minute amounts in the venom of the cone snails or analogous to the naturally available peptides, and which preferably include three disulfide bonds. The O-superfamily conotoxins include ω -conotoxins, κ -conotoxins, δ -conotoxins, μ O-conotoxins and GS conotoxin.

Thus, in one embodiment, the present invention is directed to the conotoxin peptides set forth in Table 2 and the corresponding peptides set forth in Table 1.

In a second embodiment, the present invention is directed to all of the propeptides and nucleic acid sequences encoding the propeptides or peptides set forth in Table 1.

20 In a third embodiment, the present invention is directed to derivatives or pharmaceutically acceptable salts of the conotoxin peptides disclosed herein. Examples of derivatives include peptides in which the Arg residues may be substituted by Lys, ornithine, homoarginine, nor-Lys, N-methyl-Lys, N,N-dimethyl-Lys, N,N,N-trimethyl-Lys or any synthetic basic amino acid; the Lys residues may be substituted by Arg, ornithine, homoarginine, nor-Lys, or any synthetic basic amino acid; the Tyr residues may be substituted with ¹²⁵I-Tyr, meta-Tyr, ortho-Tyr, nor-Tyr, mono-halo-Tyr, di-halo-Tyr, O-sulpho-Tyr, O-phospho-Tyr, nitro-Tyr or any synthetic hydroxy containing amino acid; the Ser residues may be substituted with Thr or any synthetic hydroxylated amino acid; the Phe residues may be substituted with any synthetic aromatic amino acid; the Trp residues may be substituted with Trp (D), neo-Trp, halo-Trp (D or L) or any aromatic synthetic amino acid; and the Asn, Ser, Thr or Hyp residues may be glycosylated. The halogen may be iodo, chloro, fluoro or bromo; preferably iodo for halogen substituted-Tyr and bromo for halogen-substituted Trp. The Tyr residues may also

be substituted with the 3-hydroxyl or 2-hydroxyl isomers (meta-Tyr or ortho-Tyr, respectively) and corresponding O-sulpho- and O-phospho-derivatives. The acidic amino acid residues may be substituted with any synthetic acidic amino acid, e.g., tetrazolyl derivatives of Gly and Ala. The aliphatic amino acids may be substituted by synthetic derivatives bearing non-natural aliphatic branched or linear side chains C_nH_{2n+2} up to and including n=8. The Leu residues may be substituted with Leu (D). The Glu residues may be substituted with Gla. The Gla residues may be substituted with Glu. The Met residues may be substituted with norleucine (Nle). The Cys residues may be in D or L configuration and may optionally be substituted with homocysteine (D or L).

Examples of synthetic aromatic amino acid include, but are not limited to, nitro-Phe, 4-substituted-Phe wherein the substituent is C_1 - C_3 alkyl, carboxyl, hydroxymethyl, sulphomethyl, halo, phenyl, -CHO, -CN, -SO₃H and -NHAc. Examples of synthetic hydroxy containing amino acid, include, but are not limited to, such as 4-hydroxymethyl-Phe, 4-hydroxyphenyl-Gly, 2,6-dimethyl-Tyr and 5-amino-Tyr. Examples of synthetic basic amino acids include, but are not limited to, N-1-(2-pyrazolinyl)-Arg, 2-(4-piperidinyl)-Gly, 2-(4-piperidinyl)-Ala, 2-[3-(2S)pyrrolidinyl]-Gly and 2-[3-(2S)pyrrolidinyl]-Ala. These and other synthetic basic amino acids, synthetic hydroxy containing amino acids or synthetic aromatic amino acids are described in Building Block Index, Version 3.0 (1999 Catalog, pages 4-47 for hydroxy containing amino acids and aromatic amino acids and pages 66-87 for basic amino acids; see also <http://www.amino-acids.com>), incorporated herein by reference, by and available from RSP Amino Acid Analogues, Inc., Worcester, MA. The residues containing protecting groups are deprotected using conventional techniques. Examples of synthetic acid amino acids include those derivatives bearing acidic functionality, including carboxyl, phosphate, sulfonate and synthetic tetrazolyl derivatives such as described by Ornstein et al. (1993) and in U.S. Patent No. 5,331,001, each incorporated herein by reference.

Optionally, in the peptides of the present invention, the Asn residues may be modified to contain an N-glycan and the Ser, Thr and Hyp residues may be modified to contain an O-glycan (e.g., g-N, g-S, g-T and g-Hyp). In accordance with the present invention, a glycan shall mean any N-, S- or O-linked mono-, di-, tri-, poly- or oligosaccharide that can be attached to any hydroxy, amino or thiol group of natural or modified amino acids by synthetic or enzymatic methodologies known in the art. The monosaccharides making up the glycan can include D-allose, D-altrose, D-glucose, D-mannose, D-gulose, D-idose, D-galactose, D-talose, D-galactosamine, D-glucosamine, D-N-acetyl-glucosamine (GlcNAc), D-N-acetyl-galactosamine (GalNAc), D-fucose or D-arabinose.

These saccharides may be structurally modified, e.g., with one or more O-sulfate, O-phosphate, O-acetyl or acidic groups, such as sialic acid, including combinations thereof. The glycan may also include similar polyhydroxy groups, such as D-penicillamine 2,5 and halogenated derivatives thereof or polypropylene glycol derivatives. The glycosidic linkage is beta and 1-4 or 1-3, preferably 1-3. The linkage between the glycan and the amino acid may be alpha or beta, preferably alpha and is 1-.

Core O-glycans have been described by Van de Steen et al. (1998), incorporated herein by reference. Mucin type O-linked oligosaccharides are attached to Ser or Thr (or other hydroxylated residues of the present peptides) by a GalNAc residue. The monosaccharide building blocks and the linkage attached to this first GalNAc residue define the "core glycans," of which eight have been identified. The type of glycosidic linkage (orientation and connectivities) are defined for each core glycan. Suitable glycans and glycan analogs are described further in U.S. Serial No. 09/420,797 filed 19 October 1999 and in PCT Application No. PCT/US99/24380 filed 19 October 1999 (PCT Published Application No. WO 00/23092), each incorporated herein by reference. A preferred glycan is Gal(β 1 \rightarrow 3)GalNAc(α 1 \rightarrow).

Optionally, in the peptides of general formula I and the specific peptides described herein, pairs of Cys residues may be replaced pairwise with isoteric lactam or ester-thioether replacements, such as Ser/(Glu or Asp), Lys/(Glu or Asp), Cys/(Glu or Asp) or Cys/Ala combinations. Sequential coupling by known methods (Barnay et al., 2000; Hruby et al., 1994; Bitan et al., 1997) allows replacement of native Cys bridges with lactam bridges. Thioether analogs may be readily synthesized using halo-Ala residues commercially available from RSP Amino Acid Analogues.

The present invention is further directed to derivatives of the above peptides and peptide derivatives which are acyclic permutations in which the cyclic permutants retain the native bridging pattern of native toxin. See, Craik et al. (2001).

In a fourth embodiment, the present invention is directed to uses of the conotoxin peptides described herein. In one aspect of this embodiment, members of the O-Superfamily conotoxins disclosed herein or a pharmaceutically acceptable salt or solvate thereof are used for regulating the flow of sodium ions through Na⁺ channels. Disorders which can be treated using these conopeptides include multiple sclerosis, other demyelinating diseases (such as acute disseminated encephalomyelitis, optic neuromyelitis, adrenoleukodystrophy, acute transverse myelitis, progressive multifocal leukoencephalopathy), sub-acute sclerosing panencephalomyelitis (SSPE), metachromatic leukodystrophy, Pelizaeus-Merzbacher disease, spinal cord injury, botulinum toxin

poisoning, Huntington's chorea, compression and entrapment neurophathies (such as carpal tunnel syndrome, ulnar nerve palsy), cardiovascular disorders (such as cardiac arrhythmias, congestive heart failure), reactive gliosis, hyperglycemia, immunosuppression, cocaine addiction, cancer, cognitive dysfunction, disorders resulting from defects in neurotransmitter release (such as Eaton-Lambert syndrome), and reversal of the actions of curare and other neuromuscular blocking drugs.

In a second aspect of this embodiment, a method of treating disorders associated with voltage gated ion channel disorders in a subject is provided which comprises administering to the subject an effective amount of the pharmaceutical composition comprising a therapeutically effective amount of a member of the O-Superfamily conotoxins described herein or a pharmaceutically acceptable salt or solvate thereof. Thus, these peptides can be used to treat neurologic disorders, such as anticonvulsant agents, or as neuroprotective agents, such as for treating stroke, or as cardiovascular agents or for the management of pain. These peptides can further be used to treat spasticity, spinal cord injury or upper motor neuron syndrome.

In a third aspect of this embodiment, a method of reducing/alleviating/decreasing the perception of pain by a subject or for inducing analgesia, particularly local analgesia, in a subject is provided which comprises administering to the subject an effective amount of the pharmaceutical composition comprising a therapeutically effective amount of a member of the O-Superfamily conotoxins described herein or a pharmaceutically acceptable salt or solvate thereof.

In a fourth aspect of this embodiment, a method for activating (i.e., opening) ATP-sensitive K^+ channels in a subject is provided which comprises administering to the subject an effective amount of the pharmaceutical composition comprising a therapeutically effective amount of a member of the O-Superfamily conotoxins described herein or a pharmaceutically acceptable salt or solvate thereof.

In a fifth aspect of this embodiment, a method of treating disorders and conditions associated with proton-gated ion channels in a subject comprising administering to the subject an effective amount of the pharmaceutical composition comprising a therapeutically effective amount of a member of the O-Superfamily conotoxins described herein or a pharmaceutically acceptable salt or solvate thereof.

Another embodiment of the invention contemplates a method of identifying compounds that mimic the therapeutic activity of the instant peptide, comprising the steps of: (a) conducting a biological assay on a test compound to determine the therapeutic activity; and (b) comparing the results obtained from the biological assay of the test compound to the results obtained from the

biological assay of the peptide. The peptide is labeled with any conventional label, preferably a radioiodine on an available Tyr. Thus, the invention is also directed to radioiodinated O-Superfamily conotoxins.

5 DETAILED DESCRIPTION OF THE PREFERRED EMBODIMENT

The invention relates to relatively short peptides (termed O-Superfamily conotoxins herein), about 20-40 residues in length, which are naturally available in minute amounts in the venom of the cone snails or analogous to the naturally available peptides, and which preferably include three disulfide bonds.

10 The present invention, in another aspect, relates to a pharmaceutical composition comprising an effective amount of an O-Superfamily conotoxin peptide, a mutein thereof, an analog thereof, an active fragment thereof or pharmaceutically acceptable salts.

15 In one embodiment, such a pharmaceutical composition comprises a member of the O-Superfamily conotoxins described herein which has the capability of delaying inactivation of sodium channels. The activity of δ -conotoxin peptides, members of the O-Superfamily, on sodium channels is described in U.S. Patent No. 5,739,276, incorporated herein by reference. The treatment of disorders according to this embodiment comprises the step of administering to such a living animal body, including a human, in need thereof a therapeutically effective amount of a pharmaceutical composition of the present invention.

20 Sodium channels comprise a large and diverse group of proteins that, through maintenance of the cellular membrane potential, are fundamental in normal biological function. The therapeutic applications for compounds that regulate the flow of sodium ions through Na^+ channels are far-reaching and include treatments of a wide range of disease and injury states. Disorders which can be treated using these conopeptides include multiple sclerosis, other demyelinating diseases (such as acute disseminated encephalomyelitis, optic neuromyelitis, adrenoleukodystrophy, acute transverse myelitis, progressive multifocal leukoencephalopathy), sub-acute sclerosing panencephalomyelitis (SSPE), metachromatic leukodystrophy, Pelizaeus-Merzbacher disease, spinal cord injury, botulinum toxin poisoning, Huntington's chorea, compression and entrapment neurophathies (such as carpal tunnel syndrome, ulnar nerve palsy), cardiovascular disorders (such as cardiac arrhythmias, congestive heart failure), reactive gliosis, hyperglycemia, immunosuppression, cocaine addiction, cancer, cognitive dysfunction, disorders resulting from

defects in neurotransmitter release (such as Eaton-Lambert syndrome), and reversal of the actions of curare and other neuromuscular blocking drugs.

In a second embodiment, such a pharmaceutical composition comprises a member of the O-Superfamily conotoxins described herein which has the capability of acting at voltage gated ion channels, particularly calcium channels, and are thus useful for treating a disorder or disease of a living animal body, including a human, which disorder or disease is responsive to the partial or complete blockade of voltage gated ion channels of the central nervous system. The activity of ω -conotoxin peptides, members of the O-Superfamily, on calcium channels is described in U.S. Patent Nos. 5,587,454; 5,559,095 and 5,824,645, incorporated herein by reference. The treatment according to this embodiment comprises the step of administering to such a living animal body, including a human, in need thereof a therapeutically effective amount of a pharmaceutical composition of the present invention.

Voltage-gated calcium channels are present in neurons, and in cardiac, smooth, and skeletal muscle and other excitable cells, and are known to play a variety of roles in membrane excitability, muscle contraction, and cellular secretion, such as in synaptic transmission (McCleskey). In neuronal cells, voltage-gated calcium channels have been classified by their electrophysiological as well as by their biochemical (binding) properties. Six classes of physiologically distinct calcium channels have been identified to date, namely the T, L, N, P, Q, and R-type channels.

It is well known that an accumulation of calcium (calcium overload) in the brain is seen after anoxia, ischemia, migraine and other hyperactivity periods of the brain, such as after epileptic convulsions. An uncontrolled high concentration of calcium in the cells of the central nervous system (CNS) is known to cause most of the degenerative changes connected with the above diseases. Compounds which can block the calcium channels of brain cells are therefore useful in the treatment of stroke, anoxia, ischemia, migraine, psychosis, or epilepsy, any other convulsive disorder and in the prevention of the degenerative changes connected with the same.

Compounds blocking the so called L-type calcium channels in the CNS are useful for the treatment of the above disorders by directly blocking the calcium uptake in the CNS. Further, it is well known that the so called N- and P-types of calcium channels, as well as possibly other types of calcium channels, are involved in the regulation of neurotransmitter release. Compounds blocking the N- and/or P-types of calcium channels indirectly and very powerfully prevent calcium overload in the CNS after the hyperactivity periods of the brain as described above by inhibiting the enhanced neurotransmitter release seen after such hyperactivity periods of the CNS, and especially the

neurotoxic, enhanced glutamate release after such hyperactivity periods of the CNS. Furthermore, blockers of the N- and/or P-types of calcium channels, as dependent upon the selectivity of the compound in question, inhibit the release of various other neurotransmitters such as aspartate, GABA, glycine, dopamine, serotonin and noradrenaline.

5 Thus, the pharmaceutical compositions comprising a member of the O-Superfamily conotoxins of the present invention are useful as neuroprotectants, cardiovascular agents, anticonvulsants, analgesics or adjuvants to general anesthetics. A "neurological disorder or disease" is a disorder or disease of the nervous system including, but not limited to, global and focal ischemic and hemorrhagic stroke, head trauma, spinal cord injury, hypoxia-induced nerve cell damage as in 10 cardiac arrest or neonatal distress or epilepsy. In addition, a "neurological disorder or disease" is a disease state and condition in which a neuroprotectant, anticonvulsant, analgesic and/or as an adjunct in general anesthesia may be indicated, useful, recommended or prescribed.

More specifically, the present invention is directed to the use of a member of the O-Superfamily conotoxins for the treatment and alleviation of epilepsy and as a general anticonvulsant 15 agent. The present invention is also directed to the use of these compounds for reducing neurotoxic injury associated with conditions of hypoxia, anoxia or ischemia which typically follows stroke, cerebrovascular accident, brain or spinal cord trauma, myocardial infarct, physical trauma, drowning, suffocation, perinatal asphyxia, or hypoglycemic events. The present invention is further directed to the use of O-superfamily-conotoxin peptides for treating pain, including acute and 20 chronic pain, such migraine, nociceptive and neuropathic pain. These peptides can further be used to treat spasticity, spinal cord injury or upper motor neuron syndrome. Other uses of these compounds are described in U.S. Patent No. 5,859,186, incorporated herein by reference.

A "neuroprotectant" is a compound capable of preventing the neuronal death associated with 25 a neurological disorder or disease. An "anticonvulsant" is a compound capable of reducing convulsions produced by conditions such as simple partial seizures, complex partial seizures, status epilepticus, and trauma-induced seizures such as occur following head injury, including head surgery. An "analgesic" is a compound capable of relieving pain by altering perception of nociceptive stimuli without producing anesthesia or loss of consciousness. A "muscle relaxant" is 30 a compound that reduces muscular tension. A "adjunct in general anesthesia" is a compound useful in conjunction with anesthetic agents in producing the loss of ability to perceive pain associated with the loss of consciousness.

The invention relates as well to methods useful for treatment of neurological disorders and diseases, including, but not limited to, global and focal ischemic and hemorrhagic stroke, head trauma, spinal cord injury, hypoxia-induced nerve cell damage such as in cardiac arrest or neonatal distress, epilepsy or other convulsive disorders without undesirable side effects.

5 Thus, in one aspect, the invention provides a method of reducing/alleviating/ decreasing the perception of pain by a subject or for inducing analgesia in a subject comprising administering to the subject an effective amount of the pharmaceutical composition comprising a therapeutically effective amount of a member of the O-Superfamily conotoxins of the present invention or a pharmaceutically acceptable salt or solvate thereof. The pain may be acute, persistent, inflammatory
10 or neuropathic pain.

15 In a second aspect, the invention provides a method of treating stroke, head or spinal cord trauma or injury, anoxia, hypoxia-induced nerve cell damage, ischemia, migraine, psychosis, anxiety, schizophrenia, inflammation, movement disorder, epilepsy, any other convulsive disorder or in the prevention of the degenerative changes connected with the same in a subject comprising administering to the subject an effective amount of the pharmaceutical composition comprising a therapeutically effective amount of a member of the O-Superfamily conotoxins of the present invention or a pharmaceutically acceptable salt or solvate thereof.

20 In a third embodiment, such a pharmaceutical composition comprises a member of the O-Superfamily conotoxins described herein which is useful as a local anesthetic for treating pain. These conopeptides have long lasting anesthetic activity and are particularly useful for spinal anesthesia, either administered acutely for post-operative pain or via an intrathecal pump for severe chronic pain situations or for treatment of pain in epithelial tissue. The activity of μ O-conotoxin peptides, members of the O-Superfamily, on sodium channels is described in U.S. Patent Application No. 09/590,386 (International Application No. PCT/US00/15779) filed on 9 June 2000,
25 incorporated herein by reference. The treatment according to this embodiment comprises the step of administering to such a living animal body, including a human, in need thereof a therapeutically effective amount of a pharmaceutical composition of the present invention.

30 More specifically, in one aspect, the pain results from surgical or medical procedures, and a member of the O-Superfamily conotoxins as described herein is administered to the central nervous system (CNS), e.g. to the spine for spinal analgesia. In a second aspect, the pain is in an epithelial tissue region associated with damage or loss of epithelial tissue as a result of, for example, plastic surgery, canker sores, burns, sore throats, genital lesions, upper or lower gastrointestinal

bronchoscopy or endoscopy, intubation, dermatologic abrasions or chemical skin peels, and a member of the O-Superfamily conotoxins as described herein is administered to alleviate the associated pain.

In a fourth embodiment, such a pharmaceutical composition comprises a member of the O-Superfamily conotoxins which has the capability of activating (i.e., opening) ATP-sensitive K⁺ channels, and is thus useful for treating a disorder or disease of a living animal body, including a human, which disorder or disease is responsive to the activation of ATP-sensitive K⁺ channels. The activity of κ-conotoxin peptides, members of the O-Superfamily, on sodium channels is described in U.S. Patent Application No. _____ (International Application No. 5 PCT/US00/25827) filed on 21 September 2000, incorporated herein by reference. The treatment according to this embodiment comprises the step of administering to such a living animal body, including a human, in need thereof a therapeutically effective amount of a pharmaceutical composition of the present invention. Thus the invention provides a method for treating cardiac ischemia, neuronal ischemia, ocular ischemia or asthma in a subject comprising administering to the subject an effective amount of the pharmaceutical composition comprising a therapeutically effective amount of a member of the O-Superfamily conotoxins described herein or a pharmaceutically acceptable salt or solvate thereof.

In a fifth embodiment, such a pharmaceutical composition comprises a member of the O-Superfamily conotoxins which has the capability of acting on proton gated ion channels, and is thus useful for treating a disorder, disease or condition of a living animal body, including a human, which disorder, disease or condition is responsive to the partial or complete blockade of proton-gated ion channels. Since, these members of the O-Superfamily antagonize the proton-gated ion channel, they are useful as analgesics, especially for pain associated with inflammation, hematomas, cardiac or muscle ischemia, or cancer. Thus, in one aspect of the present invention, the peptides and derivatives disclosed herein are useful as analgesics, i.e., for the reduction in the perception of pain or the induction of analgesia. The treatment according to this embodiment comprises the step of administering to such a living animal body, including a human, in need thereof a therapeutically effective amount of a pharmaceutical composition of the present invention.

The conotoxin peptides of the present invention are identified by isolation from *Conus* venom. Alternatively, the conotoxin peptides of the present invention are identified using recombinant DNA techniques by screening cDNA libraries of various *Conus* species using conventional techniques, such as the use of reverse-transcriptase polymerase chain reaction (RT-

PCR) or the use of degenerate probes. Primers for RT-PCR are based on conserved sequences in the signal sequence and 3' untranslated region of the conotoxin peptides genes isolated using degenerate probes. Clones which hybridize to degenerate probes are analyzed to identify those which meet minimal size requirements, i.e., clones having approximately 300 nucleotides (for a propeptide), as determined using PCR primers which flank the cDNA cloning sites for the specific cDNA library being examined. These minimal-sized clones and the clones produced by RT-PCR are then sequenced. The sequences are then examined for the presence of a peptide having the characteristics noted above for the O-Superfamily conotoxin peptides.

The conotoxin peptides described herein are sufficiently small to be chemically synthesized.

10 General chemical syntheses for preparing the foregoing conotoxin peptides are described hereinafter. Various ones of the conotoxin peptides can also be obtained by isolation and purification from specific *Conus* species using the technique described in U.S. Patent Nos. 4,447,356 (Olivera et al., 1984); 5,514,774; 5,719,264; and 5,591,821, as well as in PCT published application WO 98/03189, the disclosures of which are incorporated herein by reference.

15 Although the conotoxin peptides of the present invention can be obtained by purification from cone snails, because the amounts of conotoxin peptides obtainable from individual snails are very small, the desired substantially pure conotoxin peptides are best practically obtained in commercially valuable amounts by chemical synthesis using solid-phase strategy. For example, the yield from a single cone snail may be about 10 micrograms or less of conotoxin peptide. By 20 "substantially pure" is meant that the peptide is present in the substantial absence of other biological molecules of the same type; it is preferably present in an amount of at least about 85% purity and preferably at least about 95% purity. Chemical synthesis of biologically active conotoxin peptides depends of course upon correct determination of the amino acid sequence.

25 The conotoxin peptides can also be produced by recombinant DNA techniques well known in the art. Such techniques are described by Sambrook et al. (1989). A gene of interest (i.e., a gene that encodes a suitable conotoxin peptide) can be inserted into a cloning site of a suitable expression vector by using standard techniques. These techniques are well known to those skilled in the art. The expression vector containing the gene of interest may then be used to transfet the desired cell line. Standard transfection techniques such as calcium phosphate co-precipitation, DEAE-dextran 30 transfection or electroporation may be utilized. A wide variety of host/expression vector combinations may be used to express a gene encoding a conotoxin peptide of interest. Such

combinations are well known to a skilled artisan. The peptides produced in this manner are isolated, reduced if necessary, and oxidized to form the correct disulfide bonds.

One method of forming disulfide bonds in the conotoxin peptides of the present invention is the air oxidation of the linear peptides for prolonged periods under cold room temperatures or at room temperature. This procedure results in the creation of a substantial amount of the bioactive, disulfide-linked peptides. The oxidized peptides are fractionated using reverse-phase high performance liquid chromatography (HPLC) or the like, to separate peptides having different linked configurations. Thereafter, either by comparing these fractions with the elution of the native material or by using a simple assay, the particular fraction having the correct linkage for maximum biological potency is easily determined. However, because of the dilution resulting from the presence of other fractions of less biopotency, a somewhat higher dosage may be required.

The peptides are synthesized by a suitable method, such as by exclusively solid-phase techniques, by partial solid-phase techniques, by fragment condensation or by classical solution couplings.

In conventional solution phase peptide synthesis, the peptide chain can be prepared by a series of coupling reactions in which constituent amino acids are added to the growing peptide chain in the desired sequence. Use of various coupling reagents, e.g., dicyclohexylcarbodiimide or diisopropylcarbonyldimidazole, various active esters, e.g., esters of N-hydroxyphthalimide or N-hydroxy-succinimide, and the various cleavage reagents, to carry out reaction in solution, with subsequent isolation and purification of intermediates, is well known classical peptide methodology. Classical solution synthesis is described in detail in the treatise, "Methoden der Organischen Chemie (Houben-Weyl): Synthese von Peptiden," (1974). Techniques of exclusively solid-phase synthesis are set forth in the textbook, "Solid-Phase Peptide Synthesis," (Stewart and Young, 1969), and are exemplified by the disclosure of U.S. Patent 4,105,603 (Vale et al., 1978). The fragment condensation method of synthesis is exemplified in U.S. Patent 3,972,859 (1976). Other available syntheses are exemplified by U.S. Patents No. 3,842,067 (1974) and 3,862,925 (1975). The synthesis of peptides containing γ -carboxyglutamic acid residues is exemplified by Rivier et al. (1987), Nishiuchi et al. (1993) and Zhou et al. (1996).

Common to such chemical syntheses is the protection of the labile side chain groups of the various amino acid moieties with suitable protecting groups which will prevent a chemical reaction from occurring at that site until the group is ultimately removed. Usually also common is the protection of an α -amino group on an amino acid or a fragment while that entity reacts at the

carboxyl group, followed by the selective removal of the α -amino protecting group to allow subsequent reaction to take place at that location. Accordingly, it is common that, as a step in such a synthesis, an intermediate compound is produced which includes each of the amino acid residues located in its desired sequence in the peptide chain with appropriate side-chain protecting groups linked to various ones of the residues having labile side chains.

As far as the selection of a side chain amino protecting group is concerned, generally one is chosen which is not removed during deprotection of the α -amino groups during the synthesis. However, for some amino acids, e.g., His, protection is not generally necessary. In selecting a particular side chain protecting group to be used in the synthesis of the peptides, the following general rules are followed: (a) the protecting group preferably retains its protecting properties and is not split off under coupling conditions, (b) the protecting group should be stable under the reaction conditions selected for removing the α -amino protecting group at each step of the synthesis, and (c) the side chain protecting group must be removable, upon the completion of the synthesis containing the desired amino acid sequence, under reaction conditions that will not undesirably alter the peptide chain.

It should be possible to prepare many, or even all, of these peptides using recombinant DNA technology. However, when peptides are not so prepared, they are preferably prepared using the Merrifield solid-phase synthesis, although other equivalent chemical syntheses known in the art can also be used as previously mentioned. Solid-phase synthesis is commenced from the C-terminus of the peptide by coupling a protected α -amino acid to a suitable resin. Such a starting material can be prepared by attaching an α -amino-protected amino acid by an ester linkage to a chloromethylated resin or a hydroxymethyl resin, or by an amide bond to a benzhydrylamine (BHA) resin or para-methylbenzhydrylamine (MBHA) resin. Preparation of the hydroxymethyl resin is described by Bodansky et al. (1966). Chloromethylated resins are commercially available from Bio Rad Laboratories (Richmond, CA) and from Lab. Systems, Inc. The preparation of such a resin is described by Stewart and Young (1969). BHA and MBHA resin supports are commercially available, and are generally used when the desired polypeptide being synthesized has an unsubstituted amide at the C-terminus. Thus, solid resin supports may be any of those known in the art, such as one having the formulae $-O-CH_2$ -resin support, $-NH$ BHA resin support, or $-NH$ -MBHA resin support. When the unsubstituted amide is desired, use of a BHA or MBHA resin is preferred, because cleavage directly gives the amide. In case the N-methyl amide is desired, it can be generated from an N-methyl BHA resin. Should other substituted amides be desired, the teaching

of U.S. Patent No. 4,569,967 (Kornreich et al., 1986) can be used, or should still other groups than the free acid be desired at the C-terminus, it may be preferable to synthesize the peptide using classical methods as set forth in the Houben-Weyl text (1974).

The C-terminal amino acid, protected by Boc or Fmoc and by a side-chain protecting group, 5 if appropriate, can be first coupled to a chloromethylated resin according to the procedure set forth in K. Horiki et al. (1978), using KF in DMF at about 60°C for 24 hours with stirring, when a peptide having free acid at the C-terminus is to be synthesized. Following the coupling of the BOC-protected amino acid to the resin support, the α -amino protecting group is removed, as by using trifluoroacetic acid (TFA) in methylene chloride or TFA alone. The deprotection is carried out at 10 a temperature between about 0°C and room temperature. Other standard cleaving reagents, such as HCl in dioxane, and conditions for removal of specific α -amino protecting groups may be used as described in Schroder & Lubke (1965).

After removal of the α -amino-protecting group, the remaining α -amino- and side chain-protected amino acids are coupled step-wise in the desired order to obtain the intermediate compound defined hereinbefore, or as an alternative to adding each amino acid separately in the synthesis, some of them may be coupled to one another prior to addition to the solid phase reactor. Selection of an appropriate coupling reagent is within the skill of the art. Particularly suitable as a coupling reagent is N,N'-dicyclohexylcarbodiimide (DCC, DIC, HBTU, HATU, TBTU in the presence of HOEt or HOAt).

20 The activating reagents used in the solid phase synthesis of the peptides are well known in the peptide art. Examples of suitable activating reagents are carbodiimides, such as N,N'-diisopropylcarbodiimide and N-ethyl-N'-(3-dimethylaminopropyl)carbodiimide. Other activating reagents and their use in peptide coupling are described by Schroder & Lubke (1965) and Kapoor (1970).

25 Each protected amino acid or amino acid sequence is introduced into the solid-phase reactor in about a twofold or more excess, and the coupling may be carried out in a medium of dimethylformamide (DMF):CH₂Cl₂ (1:1) or in DMF or CH₂Cl₂ alone. In cases where intermediate coupling occurs, the coupling procedure is repeated before removal of the α -amino protecting group prior to the coupling of the next amino acid. The success of the coupling reaction at each stage of 30 the synthesis, if performed manually, is preferably monitored by the ninhydrin reaction, as described by Kaiser et al. (1970). Coupling reactions can be performed automatically, as on a Beckman 990 automatic synthesizer, using a program such as that reported in Rivier et al. (1978).

After the desired amino acid sequence has been completed, the intermediate peptide can be removed from the resin support by treatment with a reagent, such as liquid hydrogen fluoride or TFA (if using Fmoc chemistry), which not only cleaves the peptide from the resin but also cleaves all remaining side chain protecting groups and also the α -amino protecting group at the N-terminus

5 if it was not previously removed to obtain the peptide in the form of the free acid. If Met is present in the sequence, the Boc protecting group is preferably first removed using trifluoroacetic acid (TFA)/ethanedithiol prior to cleaving the peptide from the resin with HF to eliminate potential S-alkylation. When using hydrogen fluoride or TFA for cleaving, one or more scavengers such as anisole, cresol, dimethyl sulfide and methylethyl sulfide are included in the reaction vessel.

10 Cyclization of the linear peptide is preferably affected, as opposed to cyclizing the peptide while a part of the peptido-resin, to create bonds between Cys residues. To effect such a disulfide cyclizing linkage, fully protected peptide can be cleaved from a hydroxymethylated resin or a chloromethylated resin support by ammonolysis, as is well known in the art, to yield the fully protected amide intermediate, which is thereafter suitably cyclized and deprotected. Alternatively, deprotection, as well as cleavage of the peptide from the above resins or a benzhydrylamine (BHA) resin or a methylbenzhydrylamine (MBHA), can take place at 0 °C with hydrofluoric acid (HF) or TFA, followed by oxidation as described above.

15 The peptides are also synthesized using an automatic synthesizer. Amino acids are sequentially coupled to an MBHA Rink resin (typically 100 mg of resin) beginning at the C-terminus using an Advanced Chemtech 357 Automatic Peptide Synthesizer. Couplings are carried 20 out using 1,3-diisopropylcarbodiimide in N-methylpyrrolidinone (NMP) or by 2-(1H-benzotriazole-1-yl)-1,1,3,3-tetramethyluronium hexafluorophosphate (HBTU) and diethylisopro- pylethylamine (DIEA). The Fmoc protecting group is removed by treatment with a 20% solution of piperidine in dimethylformamide (DMF). Resins are subsequently washed with DMF (twice), followed by 25 methanol and NMP.

30 Muteins, analogs or active fragments, of the foregoing α conotoxin peptides are also contemplated here. See, e.g., Hammerland et al, Eur. J. Pharmacol., 226, pp. 239-244 (1992). Derivative muteins, analogs or active fragments of the conotoxin peptides may be synthesized according to known techniques, including conservative amino acid substitutions, such as outlined 35 in U.S. Pat. Nos. 5,545,723 (see particularly col. 2, line 50--col. 3, line 8); 5,534,615 (see particularly col. 19, line 45--col. 22, line 33); and 5,364,769 (see particularly col. 4, line 55--col. 7, line 26), each herein incorporated by reference.

Pharmaceutical compositions containing a compound of the present invention or its pharmaceutically acceptable salts or solvates as the active ingredient can be prepared according to conventional pharmaceutical compounding techniques. See, for example, *Remington's Pharmaceutical Sciences*, 18th Ed. (1990, Mack Publishing Co., Easton, PA). Typically, an 5 antagonistic amount of the active ingredient will be admixed with a pharmaceutically acceptable carrier. The carrier may take a wide variety of forms depending on the form of preparation desired for administration, e.g., intravenous, oral or parenteral. The compositions may further contain antioxidantizing agents, stabilizing agents, preservatives and the like. For examples of delivery methods see U.S. Patent No. 5,844,077, incorporated herein by reference.

10 "Pharmaceutical composition" means physically discrete coherent portions suitable for medical administration. "Pharmaceutical composition in dosage unit form" means physically discrete coherent units suitable for medical administration, each containing a daily dose or a multiple (up to four times) or a sub-multiple (down to a fortieth) of a daily dose of the active compound in association with a carrier and/or enclosed within an envelope. Whether the 15 composition contains a daily dose, or for example, a half, a third or a quarter of a daily dose, will depend on whether the pharmaceutical composition is to be administered once or, for example, twice, three times or four times a day, respectively.

20 The term "salt", as used herein, denotes acidic and/or basic salts, formed with inorganic or organic acids and/or bases, preferably basic salts. While pharmaceutically acceptable salts are preferred, particularly when employing the compounds of the invention as medicaments, other salts find utility, for example, in processing these compounds, or where non-medicament-type uses are contemplated. Salts of these compounds may be prepared by art-recognized techniques.

25 Examples of such pharmaceutically acceptable salts include, but are not limited to, inorganic and organic addition salts, such as hydrochloride, sulphates, nitrates or phosphates and acetates, trifluoroacetates, propionates, succinates, benzoates, citrates, tartrates, fumarates, maleates, methane-sulfonates, isothionates, theophylline acetates, salicylates, respectively, or the like. Lower alkyl quaternary ammonium salts and the like are suitable, as well.

30 As used herein, the term "pharmaceutically acceptable" carrier means a non-toxic, inert solid, semi-solid liquid filler, diluent, encapsulating material, formulation auxiliary of any type, or simply a sterile aqueous medium, such as saline. Some examples of the materials that can serve as pharmaceutically acceptable carriers are sugars, such as lactose, glucose and sucrose, starches such as corn starch and potato starch, cellulose and its derivatives such as sodium carboxymethyl

cellulose, ethyl cellulose and cellulose acetate; powdered tragacanth; malt, gelatin, talc; excipients such as cocoa butter and suppository waxes; oils such as peanut oil, cottonseed oil, safflower oil, sesame oil, olive oil, corn oil and soybean oil; glycols, such as propylene glycol, polyols such as glycerin, sorbitol, mannitol and polyethylene glycol; esters such as ethyl oleate and ethyl laurate, agar; buffering agents such as magnesium hydroxide and aluminum hydroxide; alginic acid; pyrogen-free water; isotonic saline, Ringer's solution; ethyl alcohol and phosphate buffer solutions, as well as other non-toxic compatible substances used in pharmaceutical formulations.

5 Wetting agents, emulsifiers and lubricants such as sodium lauryl sulfate and magnesium stearate, as well as coloring agents, releasing agents, coating agents, sweetening, flavoring and 10 perfuming agents, preservatives and antioxidants can also be present in the composition, according to the judgment of the formulator. Examples of pharmaceutically acceptable antioxidants include, but are not limited to, water soluble antioxidants such as ascorbic acid, cysteine hydrochloride, sodium bisulfite, sodium metabisulfite, sodium sulfite, and the like; oil soluble antioxidants, such as ascorbyl palmitate, butylated hydroxyanisole (BHA), butylated hydroxytoluene (BHT), lecithin, 15 propyl gallate, aloha-tocopherol and the like; and the metal chelating agents such as citric acid, ethylenediamine tetraacetic acid (EDTA), sorbitol, tartaric acid, phosphoric acid and the like.

20 For oral administration, the compounds can be formulated into solid or liquid preparations such as capsules, pills, tablets, lozenges, melts, powders, suspensions or emulsions. In preparing the compositions in oral dosage form, any of the usual pharmaceutical media may be employed, such as, for example, water, glycols, oils, alcohols, flavoring agents, preservatives, coloring agents, suspending agents, and the like in the case of oral liquid preparations (such as, for example, suspensions, elixirs and solutions); or carriers such as starches, sugars, diluents, granulating agents, lubricants, binders, disintegrating agents and the like in the case of oral solid preparations (such as, for example, powders, capsules and tablets). Because of their ease in administration, tablets and 25 capsules represent the most advantageous oral dosage unit form, in which case solid pharmaceutical carriers are obviously employed. If desired, tablets may be sugar-coated or enteric-coated by standard techniques. The active agent can be encapsulated to make it stable to passage through the gastrointestinal tract while at the same time allowing for passage across the blood brain barrier. See for example, WO 96/11698.

30 For parenteral administration, the compound may be dissolved in a pharmaceutical carrier and administered as either a solution or a suspension. Illustrative of suitable carriers are water, saline, dextrose solutions, fructose solutions, ethanol, or oils of animal, vegetative or synthetic

origin. The carrier may also contain other ingredients, for example, preservatives, suspending agents, solubilizing agents, buffers and the like. When the compounds are being administered intrathecally, they may also be dissolved in cerebrospinal fluid.

A variety of administration routes are available. The particular mode selected will depend 5 of course, upon the particular drug selected, the severity of the disease state being treated and the dosage required for therapeutic efficacy. The methods of this invention, generally speaking, may be practiced using any mode of administration that is medically acceptable, meaning any mode that produces effective levels of the active compounds without causing clinically unacceptable adverse effects. Such modes of administration include oral, rectal, sublingual, topical, nasal, transdermal or 10 parenteral routes. The term "parenteral" includes subcutaneous, intravenous, epidural, irrigation, intramuscular, release pumps, or infusion.

For example, administration of the active agent according to this invention may be achieved using any suitable delivery means, including:

15 (a) pump (see, e.g., Luer & Hatton (1993), Zimm et al. (1984) and Ettinger et al. (1978));
(b), microencapsulation (see, e.g., U.S. Patent Nos. 4,352,883; 4,353,888; and 5,084,350);
(c) continuous release polymer implants (see, e.g., U.S. Patent No. 4,883,666);
(d) macroencapsulation (see, e.g., U.S. Patent Nos. 5,284,761, 5,158,881, 4,976,859 and
4,968,733 and published PCT patent applications WO92/19195, WO 95/05452);
20 (e) naked or unencapsulated cell grafts to the CNS (see, e.g., U.S. Patent Nos. 5,082,670 and
5,618,531);
(f) injection, either subcutaneously, intravenously, intra-arterially, intramuscularly, or to
other suitable site; or
(g) oral administration, in capsule, liquid, tablet, pill, or prolonged release formulation.

In one embodiment of this invention, an active agent is delivered directly into the CNS, 25 preferably to the brain ventricles, brain parenchyma, the intrathecal space or other suitable CNS location, most preferably intrathecally. This administration is preferably by a pump.

30 Alternatively, targeting therapies may be used to deliver the active agent more specifically to certain types of cell, by the use of targeting systems such as antibodies or cell specific ligands. Targeting may be desirable for a variety of reasons, e.g. if the agent is unacceptably toxic, or if it would otherwise require too high a dosage, or if it would not otherwise be able to enter the target cells.

The active agents, which are peptides, can also be administered in a cell based delivery system in which a DNA sequence encoding an active agent is introduced into cells designed for implantation in the body of the patient, especially in the spinal cord region. Suitable delivery systems are described in U.S. Patent No. 5,550,050 and published PCT Application Nos. WO 5 92/19195, WO 94/25503, WO 95/01203, WO 95/05452, WO 96/02286, WO 96/02646, WO 96/40871, WO 96/40959 and WO 97/12635. Suitable DNA sequences can be prepared synthetically for each active agent on the basis of the developed sequences and the known genetic code.

The active agent is preferably administered in a therapeutically effective amount. By a "therapeutically effective amount" or simply "effective amount" of an active compound is meant a 10 sufficient amount of the compound to treat the desired condition at a reasonable benefit/risk ratio applicable to any medical treatment. The actual amount administered, and the rate and time-course of administration, will depend on the nature and severity of the condition being treated. Prescription of treatment, e.g. decisions on dosage, timing, etc., is within the responsibility of general practitioners or specialists, and typically takes account of the disorder to be treated, the condition 15 of the individual patient, the site of delivery, the method of administration and other factors known to practitioners. Examples of techniques and protocols can be found in *Remington's Pharmaceutical Sciences*.

Dosage may be adjusted appropriately to achieve desired drug levels, locally or systemically. Typically the active agents of the present invention exhibit their effect at a dosage range from about 20 0.001 mg/kg to about 250 mg/kg, preferably from about 0.01 mg/kg to about 100 mg/kg of the active ingredient, more preferably from about 0.05 mg/kg to about 75 mg/kg. A suitable dose can be administered in multiple sub-doses per day. Typically, a dose or sub-dose may contain from about 0.1 mg to about 500 mg of the active ingredient per unit dosage form. A more preferred dosage will contain from about 0.5 mg to about 100 mg of active ingredient per unit dosage form. 25 Dosages are generally initiated at lower levels and increased until desired effects are achieved. In the event that the response in a subject is insufficient at such doses, even higher doses (or effective higher doses by a different, more localized delivery route) may be employed to the extent that patient tolerance permits. Continuous dosing over, for example 24 hours or multiple doses per day are contemplated to achieve appropriate systemic levels of compounds.

30 For the treatment of pain, if the route of administration is directly to the CNS, the dosage contemplated is from about 1 ng to about 100 mg per day, preferably from about 100 ng to about 10 mg per day, more preferably from about 1 μ g to about 100 μ g per day. If administered

peripherally, the dosage contemplated is somewhat higher, from about 100 ng to about 1000 mg per day, preferably from about 10 μ g to about 100 mg per day, more preferably from about 100 μ g to about 10 mg per day. If the conopeptide is delivered by continuous infusion (e.g., by pump delivery, biodegradable polymer delivery or cell-based delivery), then a lower dosage is contemplated than for bolus delivery.

Advantageously, the compositions are formulated as dosage units, each unit being adapted to supply a fixed dose of active ingredients. Tablets, coated tablets, capsules, ampoules and suppositories are examples of dosage forms according to the invention.

It is only necessary that the active ingredient constitute an effective amount, i.e., such that a suitable effective dosage will be consistent with the dosage form employed in single or multiple unit doses. The exact individual dosages, as well as daily dosages, are determined according to standard medical principles under the direction of a physician or veterinarian for use humans or animals.

The pharmaceutical compositions will generally contain from about 0.0001 to 99 wt. %, preferably about 0.001 to 50 wt. %, more preferably about 0.01 to 10 wt.% of the active ingredient by weight of the total composition. In addition to the active agent, the pharmaceutical compositions and medicaments can also contain other pharmaceutically active compounds. Examples of other pharmaceutically active compounds include, but are not limited to, analgesic agents, cytokines and therapeutic agents in all of the major areas of clinical medicine. When used with other pharmaceutically active compounds, the conotoxin peptides of the present invention may be delivered in the form of drug cocktails. A cocktail is a mixture of any one of the compounds useful with this invention with another drug or agent. In this embodiment, a common administration vehicle (e.g., pill, tablet, implant, pump, injectable solution, etc.) would contain both the instant composition in combination supplementary potentiating agent. The individual drugs of the cocktail are each administered in therapeutically effective amounts. A therapeutically effective amount will be determined by the parameters described above; but, in any event, is that amount which establishes a level of the drugs in the area of body where the drugs are required for a period of time which is effective in attaining the desired effects.

The practice of the present invention employs, unless otherwise indicated, conventional techniques of chemistry, molecular biology, microbiology, recombinant DNA, genetics, immunology, cell biology, cell culture and transgenic biology, which are within the skill of the art.

See, e.g., Maniatis *et al.*, 1982; Sambrook *et al.*, 1989; Ausubel *et al.*, 1992; Glover, 1985; Anand, 1992; Guthrie and Fink, 1991; Harlow and Lane, 1988; Jakoby and Pastan, 1979; *Nucleic Acid Hybridization* (B. D. Hames & S. J. Higgins eds. 1984); *Transcription And Translation* (B. D. Hames & S. J. Higgins eds. 1984); *Culture Of Animal Cells* (R. I. Freshney, Alan R. Liss, Inc., 5 1987); *Immobilized Cells And Enzymes* (IRL Press, 1986); B. Perbal, *A Practical Guide To Molecular Cloning* (1984); the treatise, *Methods In Enzymology* (Academic Press, Inc., N.Y.); *Gene Transfer Vectors For Mammalian Cells* (J. H. Miller and M. P. Calos eds., 1987, Cold Spring Harbor Laboratory); *Methods In Enzymology*, Vols. 154 and 155 (Wu *et al.* eds.), *Immunochemical Methods In Cell And Molecular Biology* (Mayer and Walker, eds., Academic Press, London, 1987); 10 *Handbook Of Experimental Immunology*, Volumes I-IV (D. M. Weir and C. C. Blackwell, eds., 1986); Riott, *Essential Immunology*, 6th Edition, Blackwell Scientific Publications, Oxford, 1988; Hogan *et al.*, Manipulating the Mouse Embryo, (Cold Spring Harbor Laboratory Press, Cold Spring Harbor, N.Y., 1986).

15

EXAMPLES

The present invention is described by reference to the following Examples, which are offered by way of illustration and are not intended to limit the invention in any manner. Standard techniques well known in the art or the techniques specifically described below were utilized.

20

EXAMPLE 1

Isolation of O-Superfamily Conotoxins

Crude venom was extracted from venom ducts (Cruz *et al.*, 1976), and the components were purified as previously described (Cartier *et al.*, 1996). The crude extract from venom ducts was purified by reverse phase liquid chromatography (RPLC) using a Vydac C₁₈ semi-preparative 25 column (10 x 250 mm). Further purification of bioactive peaks was done on a Vydac C₁₈ analytical column (4.6 x 220 mm). The effluents were monitored at 220 nm. Peaks were collected, and aliquots were assayed for activity.

The amino acid sequence of the purified peptides were determined by standard methods. The purified peptides were reduced and alkylated prior to sequencing by automated Edman degradation 30 on an Applied Biosystems 477A Protein Sequencer with a 120A Analyzer (DNA/Peptide Facility, University of Utah) (Martinez *et al.*, 1995; Shon *et al.*, 1994).

In accordance with this method, peptides δ -GmVIA, δ -PVIA, δ -SVIE, δ -SVIE [D1E], δ -NgVIA, δ -TxVIA and Israel TxVIA were obtained.

EXAMPLE 2

Synthesis of Conopeptides

The synthesis of conopeptides, either the mature toxins or the precursor peptides, was separately performed using conventional protection chemistry as described by Cartier et al. (1996). Briefly, the linear chains were built on Rink amide resin by Fmoc procedures with 2-(1H-benzotriol-1-yl)-1,1,3,3,-tetramethyluronium tetrafluoroborated coupling using an ABI model 430A peptide synthesizer with amino acid derivatives purchased from Bachem (Torrence CA). Orthogonal protection was used on cysteines: two cysteines were protected as the stable Cys(S-acetamidomethyl), while the other two cysteines were protected as the acid-labile Cys(S-trityl). After removal of the terminal Fmoc protecting group and cleavage of the peptides from the resins, the released peptides were precipitated by filtering the reaction mixture into -10°C methyl t-butyl ether, which removed the protecting groups except the Cys(S-acetamidomethyl). The peptides were dissolved in 0.1% TFA and 60% acetonitrile and purified by RPLC on a Vydac C₁₈ preparative column (22 x 250 mm) and eluted at a flow rate of 20 mL/min with a gradient of acetonitrile in 0.1% TFA.

The disulfide bridges in the three conopeptides were formed as described in Cartier et al. (1996). Briefly, the disulfide bridges between one pair of cysteines were formed by air oxidation which was judged to be complete by analytical RPLC. The monocyclic peptides were purified by RPLC on a Vydac C₁₈ preparative column (22 x 250 mm) and eluted with a gradient of acetonitrile in 0.1% TFA. Removal of S-acetamidomethyl groups and closure of the disulfide bridge between the other pair of cysteines was carried out simultaneously by iodine oxidation. The cyclic peptides were purified by RPLC on a Vydac C₁₈ preparative column (22 x 250 mm) and eluted with a gradient of acetonitrile in 0.1% TFA.

EXAMPLE 3

Isolation of DNA Encoding O-Superfamily Conotoxins

DNA coding for conotoxins described herein was isolated and cloned in accordance with conventional techniques using general procedures well known in the art, such as described in Olivera et al. (1996). Alternatively, cDNA libraries was prepared from *Conus* venom duct using

conventional techniques. DNA from single clones was amplified by conventional techniques using primers which correspond approximately to the M13 universal priming site and the M13 reverse universal priming site. Clones having a size of approximately 300-500 nucleotides were sequenced and screened for similarity in sequence to known O-Superfamily conotoxins, including the δ -conotoxins isolated in Example 1. The DNA sequences, encoded propeptide sequences and sequences of the mature toxins are set forth in the attached Table 1. DNA sequences coding for the mature toxin can also be prepared on the basis of the DNA sequences set forth on these pages. An alignment of the conotoxins is set forth in Table 2.

10

TABLE 1

**Sequences of Mature O-Superfamily Conotoxins,
Propeptides and DNA Encoding Propeptides**

15 **Name:** δ -GmVIA
Species: gloriamaris
Isolated: Yes
Cloned: Yes

DNA Sequence:

20 ATGAAACTGACGTGCATGATGATCGTTGCTGTGCTGTTCTGACCGCCTGGACATTG
 GTCACGGCTGATGACTCCGGAAATGGAATGGAGATTCTTTCCGAAGGCGGGTCA
 CGAAATGGAGAACCTCGAAGTCTCTAATCGGGTCAAGCCGTGCCGTAAGAAGGTC
 AACTTTGTGATCCGATATTCAAAACTGCTGCCGTGGCTGGAATTGCGTTCTTTCTG
 CGTCTGAAACTACCGTGATGTCTCTCCCCCTC (SEQ ID NO:1)

Translation:

MKLT CMMIVAVLFLTAWTFVTADD SGN GMEILFPKAGHE MENLEVS NRVKPCRKEGQ
 LCDPIFQNCCR GWN CVLFCV (SEQ ID NO:2)

Toxin Sequence:

30 Val-Lys-Xaa3-Cys-Arg-Lys-Xaa1-Gly-Gln-Leu-Cys-Asp-Xaa3-Ile-Phe-Gln-Asn-Cys-Cys-Arg-
 Gly-Xaa4-Asn-Cys-Val-Leu-Phe-Cys-Val-[^] (SEQ ID NO:3)

35 **Name:** δ -GmVIA [F15Y]
Species: gloriamaris

Toxin Sequence:

40 Val-Lys-Xaa3-Cys-Arg-Lys-Xaa1-Gly-Gln-Leu-Cys-Asp-Xaa3-Ile-Xaa5-Gln-Asn-Cys-Cys-
 Arg-Gly-Xaa4-Asn-Cys-Val-Leu-Phe-Cys-Val-[^] (SEQ ID NO:4)

Name: δ-GmVIA [F27Y]
Species: gloriamaris
Isolated: No

5 **Toxin Sequence:**
 Val-Lys-Xaa3-Cys-Arg-Lys-Xaa1-Gly-Gln-Leu-Cys-Asp-Xaa3-Ile-Phe-Gln-Asn-Cys-Cys-Arg-
 Gly-Xaa4-Asn-Cys-Val-Leu-Xaa5-Cys-Val-^ (SEQ ID NO:5)

10 **Name:** Omaria9
Species: omaria
Isolated: No
Cloned: Yes

15 **DNA Sequence:**
 GAAGCTGGTACGCCTGCAGGTACCGGTCCCGAATTCCCGGGTCGACATCATCATCA
 TCGATCCATCTGTCCATCCATCCATTCAATTCAATTCTCGCTGCCAGACTATAATAAACATT
 CAAGTCTCTCTTCTTTGTGCTGACAGATCGATCAGGATGTGCCGTAGAGAAAGC
 TCAACTTGTGATCCGATTTCAAAACACTGCTGCCATGGCTTGTGCGTTGGTC
 TCGGTCTAAAACCTACCGTGATGTCTTCTCCTCCCTCTAGTAGTAGTAGGGCGGCCGC
 TCTAGAGGATCCAAGCTTACGTACCGTGATCGACGTCATAAGCTCTTCTATAAGTG
 TCACCTAAATTCAATTCACTGGCCGTGTTACAACGTCGTGACTGGAAAACCT
 GGC GTTACCCAACCTTAATGCCCTTGCAGCACATCCCCCTTCGCCAGCTGGCGTAAT
 AGCGAAGAGGCCCGCACCGATGCCCTCCAACAGTTGCGCAGCCTGAATGGCGA
 ATGGGACGCGCCCTGTAGCGCGCATTAT (SEQ ID NO:6)

20 **Translation:**
 SIRMCRREAQLCDPIFQNCCCHGLFCVLVCV (SEQ ID NO:7)

25 **Toxin Sequence:**
 Met-Cys-Arg-Arg-Xaa1-Ala-Gln-Leu-Cys-Asp-Xaa3-Ile-Phe-Gln-Asn-Cys-Cys-His-Gly-Leu-
 Phe-Cys-Val-Leu-Val-Cys-Val-^ (SEQ ID NO:8)

30 **Name:** Tx6.11
Species: textile
Isolated: No
Cloned: Yes

35 **DNA Sequence:**
 GGCATTACCTAAACATCACCAAGATGAAACTGACGTGCATGATGATCGTTGCTGT
 GCTGTTCTGACCGCCTGGACATTGTCACGGCTGATGACTCCAGAAATGGAATGGA
 GAATCTTTCCGAAGGCAGGTACGAAATGGAGAACCTCGAAGACTCTAAACACA
 GGCACCAGGAGAGACCGGACACCGGCGACAAAGAAGAGATGCTGCTACAGAGACA
 40 GGTCAAGCCGTGTCGAAAGAACATCAACTTTGTGATCTGATTTTCAAAACTGCTG
 CCGTGGCTGGTATTGCGTTCTGTGCACTTGAAAGCTACCTGATGTGTTCTAC
 TCCCATC (SEQ ID NO:9)

Translation:

MKLTCMMIVAVLFLTAWTFVTADDSRNGMENLFPKAGHEMENLEDSKHRHQERPDTG
DKEEMLLQRQVKPCRKEHQLCDLIFQNCCRGWYCVVLSCT (SEQ ID NO:10)

Toxin Sequence:

Xaa2-Val-Lys-Xaa3-Cys-Arg-Lys-Xaa1-His-Gln-Leu-Cys-Asp-Leu-Ile-Phe-Gln-Asn-Cys-Cys-
Arg-Gly-Xaa4-Xaa5-Cys-Val-Val-Leu-Ser-Cys-Thr-^ (SEQ ID NO:11)

10 **Name:** Om6.6
Species: omaria
Isolated: No
Cloned: Yes

15 **DNA Sequence:**
ATGAAACTGACGTGCCTGATGATCGTTGCCGTGCTGTCCTGACCGGCTGGACATT
GTCACGGCTGATGACTCTGGAAATGGATTGGGAATCTTTTCGAATGCACATCAC
GAAATGAAGAACCCCGAAGCCTCTAAATTGAACAAGAGGTGCCTTCCACACGAGGG
CCCTTGTAAATTGGCTTACACAAAAGTGCAGTGGTTATAATTGCATCATTTC
TGCCTATAAAACTACCGTGATGTCTCTTCCCCCTC (SEQ ID NO:12)

Translation:

MKLTCLMIVAVLSLTGWTFTVADDSGNGLGNLFNSNAHHEMKNPEASKLNKRCVPHEG
PCNWLTQNCCSGYNCIHFCL (SEQ ID NO:13)

Toxin Sequence:

Cys-Val-Xaa3-His-Xaa1-Gly-Xaa3-Cys-Asn-Xaa4-Leu-Thr-Gln-Asn-Cys-Ser-Gly-Xaa5-
Asn-Cys-Ile-Ile-Phe-Phe-Cys-Leu-^ (SEQ ID NO:14)

30 **Name:** Da6.2
Species: dalli
Isolated: No
Cloned: Yes

35 **DNA Sequence:**
ATGAAACTGACGTGCCTGCTGATCATTGCTGTGCTGTTCTGACCGCCTGGACATT
GTCACGGCTGATGACTCCGGAAATGGAATGGAGAATCTTTCCGAAGGCACGTCA
CGAAATGGAGAACCTCGAAGACTCTAAACACAGGCACCAGGAGAGACCGGACACG
GGCGACAAAGAAGAGATGCTGCTACAGAGACAGGTCAAGCCGTGTCGTAAAGAAC
ATCAACTTGTGATCTGATTTCAAAACTGCTGCCGTGGCTGGTATTGCTTGCITCG
TCCTTGCATCTGAAACTACCGTGATGTCTCTCCCATC (SEQ ID NO:15)

Translation:

MKLTCLLIIAVLFLTAWTFVTADDSGNGMENLFPKARHEMENLEDSKHRHQERPDTGD
KEEMLLQRQVKPCRKEHQLCDLIFQNCCRGWYCLLRPCI (SEQ ID NO:16)

Toxin Sequence:

Xaa2-Val-Lys-Xaa3-Cys-Arg-Lys-Xaa1-His-Gln-Leu-Cys-Asp-Leu-Ile-Phe-Gln-Asn-Cys-Cys-Arg-Gly-Xaa4-Xaa5-Cys-Leu-Leu-Arg-Xaa3-Cys-Ile-^ (SEQ ID NO:17)

5

Name: Da6.6

Species: dalli

Isolated: No

10 **Cloned:** Yes

DNA Sequence:

ATGAAACTGACGTGTATGCTGATCATTGCTGTGCTGTTCTTGACCGCCTGGACATTC
 GTCACGGCTGATGACTCCGAAATGGAATGGAGAATCTTTTCCGAAGGCACGTCA
 15 CGAAATGGAGAACCTCGAAGACTCTAACACACAGGCACCAGGAGAGACGGACACG
 GGCGACAAAGAACAGAGATGCTGCTACAGAGACGGGTCAAGCCGTGCAGTGAAGAAG
 GTCAACTTGTGATCCACTTCTAAAATGCTGCCGTGGCTGGCATTGCGTTCTGT
 CTCTTGCCTCTGAAACTACCGTGATGTCTCTCCCATC (SEQ ID NO:18)

20

Translation:

MKLTCLIIAVLFLTAWTFVTADDNGNGMENLFPKARHEMENLEDSKHRHQERPDTGD
 KEEMLLQRRVKPCSEEGQLCDPLSQNCCRGWHCVLVSCV (SEQ ID NO:19)

Toxin Sequence:

25 Val-Lys-Xaa3-Cys-Ser-Xaa1-Xaa1-Gly-Gln-Leu-Cys-Asp-Xaa3-Leu-Ser-Gln-Asn-Cys-Cys-Arg-Gly-Xaa4-His-Cys-Val-Leu-Val-Ser-Cys-Val-^ (SEQ ID NO:20)

25

Name: δ-TxVIA

30

Species: textile

Isolated: Yes

Cloned: Yes

DNA Sequence:

35 AAACATGCCAAGATGAAACTGACGTGCATGATGATCGTTGCTGTGCTGTTCTTGAC
 CGCCTGGACATTGCCACGGCTGATGACCCCAGAAATGGATTGGGAATCTTTTTC
 GAATGCACATCACGAAATGAAGAACCCGAAGCCTCTAAATTGAACAAGAGGTGGT
 GCAAACAAAGCGGTGAAATGTGAATTGTTAGACCAAAACTGCTGCGACGGCTAT
 TGCA TAGTACTGTCTGCACATAAAACTGCCGTGATGTCTTCTCTTCCCTCTGTGCT
 40 ACCTGGCTTGATCTTGATTGGCGCGTGTGTTCACTGGTTATGAACCCCCCCCC
 CCCCCCCCCCCCCCTCCGGCTCTGGAGGCCTGGGGGTTAACATCCAAATAA
 AGTGACAG (SEQ ID NO:21)

40

Translation:

45 MKLTCLMIVAVLFLTAWTFATADDPRNCLGNLFSNAHHEMKNPEASKLNKRWCKQS
 GEMCNLLDQNCCDGYICLVCT (SEQ ID NO:22)

Toxin Sequence:

Xaa4-Cys-Lys-Gln-Ser-Gly-Xaa1-Met-Cys-Asn-Leu-Leu-Asp-Gln-Asn-Cys-Cys-Asp-Gly-Xaa5-Cys-Ile-Val-Leu-Val-Cys-Thr-^ (SEQ ID NO:23)

5

Name: δ-TxVIA [M8J]
Species: textile

Toxin Sequence:

10 Xaa4-Cys-Lys-Gln-Ser-Gly-Xaa1-Xaa6-Cys-Asn-Leu-Leu-Asp-Gln-Asn-Cys-Cys-Asp-Gly-Xaa5-Cys-Ile-Val-Leu-Val-Cys-Thr-^ (SEQ ID NO:24)

15

Name: M6.4
Species: magus
Isolated: No
Cloned: Yes

DNA Sequence:

20 ATGAAACTGACGTGTGATGATCGTTGCTGTGCTGTTCTGACCGCCTGGACATT
 GCCACGGCTGATGACCCCCAGAAATGGATTGGGAATCTTTTTCGAATGCACATCAC
 GAAATGAAGAACCCCGAAGCCTCTAAATTGAACAAAGAGGTGGTCAAACAAAGCG
 GTGAAATGTGTAATTGTTAGACCAAAACTGCTGCGACGGCTATTGCATAGTACTTG
 TCTGCACATAAAACTGCCGTGATGTCTCTCCTCCCCTC (SEQ ID NO:25)

25

Translation:

MKLTCVMIVAVLFLTAWTFATADDPRNGLGNLFSNAHHEMKNPEASKLNKRWCKQSG
 EMCNLLDQNCCDGYCVLVCT (SEQ ID NO:26)

30

Toxin Sequence:

Xaa4-Cys-Lys-Gln-Ser-Gly-Xaa1-Met-Cys-Asn-Leu-Leu-Asp-Gln-Asn-Cys-Cys-Asp-Gly-Xaa5-Cys-Ile-Val-Leu-Val-Cys-Thr-^ (SEQ ID NO:27)

35

Name: Israel TxIA
Species: textile
Isolated: Yes
Cloned: No

40

Toxin Sequence:

Xaa4-Cys-Lys-Gln-Ser-Gly-Xaa1-Met-Cys-Asn-Leu-Leu-Asp-Gln-Asn-Cys-Cys-Asp-Gly-Xaa5-Cys-Ile-Val-Phe-Val-Cys-Thr-^ (SEQ ID NO:28)

45

Name: Di6.2
Species: distans
Isolated: No

Cloned: Yes

DNA Sequence:

ATGAAACTGACGTGCCTGATGATCGTTGCTGTGCTGTTCTTGACCGCCTGGACATT
 5 GCCACGGCTGATGACCCCAGAAATGGATTGGGAATCTTTTCGAATGCACATCAC
 GAAATGAAGAACCCCGAACGCCTCTAAATTGAACAAGAGGTGGTCAAACAAAGCG
 GTGAAATGTGTAATTGTTAGACCAAAACTGCTGCGACGGCTATTGCATAGTACTTG
 TCTGCACATAAAACTGCCGTGATGTCTTCTCCTCCCCTC (SEQ ID NO:29)

10 Translation:

MKLTCLMIVAVLFLTAWTFATADDPRNGLGNLFSNAHHEMKNPEASKLNKRWCKQSG
 EMCNLLDQNCCDGYCIVLVCT (SEQ ID NO:30)

Toxin Sequence:

15 Xaa4-Cys-Lys-Gln-Ser-Gly-Xaa1-Met-Cys-Asn-Leu-Leu-Asp-Gln-Asn-Cys-Cys-Asp-Gly-
 Xaa5-Cys-Ile-Val-Leu-Val-Cys-Thr-^ (SEQ ID NO:31)

20 Name: Af6.9

Species: ammiralis

Isolated: No

Cloned: Yes

DNA Sequence:

25 ATGAAACTGACGTGCCTGATGATCGTTGCTGTGCTGTTCTTGACCGCCTGGACATT
 GCCACGGCTGATGACCCCAGAAATGGATTGGGAATCTTTTCGAATGCACATCAC
 GAAATGAAGAACCCCGAACGCCTCTAAATTGAACAAGAGGTGGTCAAACAAAGCG
 GTGAAATGTGTAATTGTTAGACCAAAACTGCTGCGAGGGCTATTGCATAGTACTTG
 TCTGCACATAAAACTGCCGTGATGTCTTCTCCTCCCCTC (SEQ ID NO:32)

30

Translation:

MKLTCVMIVAVLFLTAWTFATADDPRNGLGNLFSNAHHEMKNPEASKLNKRWCKQSG
 EMCNLLDQNCCEGYCIVLVCT (SEQ ID NO:33)

35

Toxin Sequence:

Xaa4-Cys-Lys-Gln-Ser-Gly-Xaa1-Met-Cys-Asn-Leu-Leu-Asp-Gln-Asn-Cys-Cys-Xaa1-Gly-
 Xaa5-Cys-Ile-Val-Leu-Val-Cys-Thr-^ (SEQ ID NO:34)

40

Name: Da6.4

Species: dalli

Isolated: No

Cloned: Yes

45

DNA Sequence:

ATGAAACTGACGTGCCTGATGATCGTTGCTGTGCTGTTCTTGACCGCCTGGACATT
 GCCACGGCTGATGACCCCAGAAATGGATTGGAGAATCTTTTTGAAGGCACATCA

CGAAATGAACCCCGAAGCCTCTAAGTTGAATGAGAGGTGCCTGGTGGTGGTGAAG
 TTTGTGATATCTTTTCCACAATGCTGGCTATTGCATTCTCTTCTGCACATAA
 AACTACCGTGATGTCTCTCCTCCCCCTC (SEQ ID NO:35)

5 **Translation:**

MKLTCVMIVAVLFLTAWTFATADDPRNGLENLFLKAHHEMNPEASKLNERCLGGGEV
 CDIFFPQCCCGYCILLFCT (SEQ ID NO:36)

10 **Toxin Sequence:**

Cys-Leu-Gly-Gly-Gly-Xaa1-Val-Cys-Asp-Ile-Phe-Phe-Xaa3-Gln-Cys-Cys-Gly-Xaa5-Cys-Ile-
 Leu-Leu-Phe-Cys-Thr-^ (SEQ ID NO:37)

15 **Name:** Gm6.5
Species: gloriamaris
Isolated: No
Cloned: Yes

20 **DNA Sequence:**

GCTTGACCGTGAATTGGCTTCACAGTTTCACTGTCGTCTTGGCATCATCTGAA
 ACATGCCAAGATGAAACTGACGTGCATGATCGTTGCTGTGCTGTTCTGACCG
 CCTGGACATTGCCACGGCTGATGACCCCAGAAATGGATTGGGAATATTTTCGA
 ATGCACATCACGAAATGAAGAATCCCGAAGCCTCTAAATTGAACAAGAGGTGCCGT
 CTAGGGGCTGAAAGTTGTGATGTAATTACAAAATGCTGCCAAGGCACGTGCGT
 TTTTTCTGCTTACCATGATGTCCTATTCTCCTGTGCTACCTGGCTGATCTTC
 ATTAGCGCGTGCCTTCACTGGTTATGAACCCCTGATCCGACTCTGGCAGCCTC
 GGGGTTAACATCCAAATAAACGACAGCACAATGACAAA (SEQ ID NO:38)

25 **Translation:**

MKLTCMMIVAVLFLTAWTFATADDPRNGLGNIFSNAHHEMNPEASKLNKRCRLGAE
 SCDVISQNCCQGTCVFFCLP (SEQ ID NO:39)

30 **Toxin Sequence:**

Cys-Arg-Leu-Gly-Ala-Xaa1-Ser-Cys-Asp-Val-Ile-Ser-Gln-Asn-Cys-Cys-Gln-Gly-Thr-Cys-Val-
 Phe-Phe-Cys-Leu-Xaa3-^ (SEQ ID NO:40)

35 **Name:** Gm6.6
Species: gloriamaris
Isolated: No
Cloned: Yes

40 **DNA Sequence:**

GGATCCTTGCACGGTGAATTGGCTTCACAGTTCACTGTCGTCTTCGCATCATC
 45 CAAAACATCACCAAGATGAAACTGACGTGCATGATCGTTGCTGTGCTGTTCTG
 ACCGCCTGGACATTGCCACGGCTGATGACCCCAGAAATGGATTGGAGAAACTTT
 TTCGAATACACATCACGAAATGAAGAACCCGAAGCCTCTAAATTGAACAAGAGGT

GCAAACAAGCTGATGAATCTTGTATGTATTTCACTTGACTGCTGCACCGGCTTAT
 GCTTGGGATTCTCGTATCGTGTCTCTACTCCCTCTGTgCTACCTGGCTTGAT
 CTTGATTGGCGTGTGCCTTCATTGGTTATGAACCCCCCTGATCCGATTCTTGGCG
 GCCTCGGGGGTTCAACATCCAAATAAGCGACAGCACAATAAAAAAA (SEQ ID

5 NO:41)

Translation:

MKLT CMMIVAVLFLTAWTFATADDPRNGLEKLF SNTHHEMKNPEASKLNKRCKQADE
 SCNVFSLDCCTGLCLGFCSV (SEQ ID NO:42)

10

Toxin Sequence:

Cys-Lys-Gln-Ala-Asp-Xaa1-Ser-Cys-Asn-Val-Phe-Ser-Leu-Asp-Cys-Cys-Thr-Gly-Leu-Cys-
 Leu-Gly-Phe-Cys-Val-Ser-^ (SEQ ID NO:43)

15

Name: Gm6.3
Species: gloriamaris
Isolated: No
Cloned: Yes

20

DNA Sequence:

ATGAAACTGACGTGCATGATGATCGTTGCTGTGCTGTTCTGACCCACCTGGACATT
 GCCACGGCCATCACCAAGGAATGGATTGGGAATCTTTCCGAAGAACATCACGA
 AATGAAGAACCCCGAACGCCTCTAAATTGAACAAAGAGGTGCGTCCATACGAGGGCC
 CTTGTAATTGGCTTACACAAACTGCTGCGATGAGCTATGCGTATTCTGCCTAT
 AAAACTAGCCTGATGT (SEQ ID NO:44)

25

Translation:

MKLT CMMIVAVLFLTTWTFATAIRNGLGNLFPKNHHEMKNPEASKLNKRCVPYEGPC
 30 NWLTQNCCDELCVFFCL (SEQ ID NO:45)

30

Toxin Sequence:

Cys-Val-Xaa3-Xaa5-Xaa1-Gly-Xaa3-Cys-Asn-Xaa4-Leu-Thr-Gln-Asn-Cys-Cys-Asp-Xaa1-
 Leu-Cys-Val-Phe-Phe-Cys-Leu-^ (SEQ ID NO:46)

35

Name: M6.5
Species: magus
Isolated: No
Cloned: Yes

40

DNA Sequence:

ATGAAACTGACGTGCCTGATGATCGTTGCTGTGCTGTTCTGACCCGCTGGACATT
 GCCACGGCTGATGACTCCGAAATGGATTGGAGAAACTTTTCGAATGCACATCA
 45 CGAAATGAAGAACCCCGAACGCCTCTAAATTGAACAAAGAGGTGCAAACAAGCTGAT
 GAACCTTGTGATGTATTTCACTGAATGCTGCACCGGCATATGTCTTGGATTCTGC
 ACGTGGTGATGTCTCCCTCCCTC (SEQ ID NO:47)

Translation:

MKLTCVMIVAVLFLTIVWTFATADDSGNGLEKLFNSNAHHEMKNPEASKLNKRCKQADE
PCDVFSLECCTGICLGFCTW (SEQ ID NO:48)

Toxin Sequence:

Cys-Lys-Gln-Ala-Asp-Xaa1-Xaa3-Cys-Asp-Val-Phe-Ser-Leu-Xaa1-Cys-Cys-Thr-Gly-Ile-Cys-
Leu-Gly-Phe-Cys-Thr-Xaa4-^ (SEQ ID NO:49)

10 **Name:** Tx6.2
Species: textile
Isolated: No
Cloned: Yes

DNA Sequence:

GCCTTGACCGGTGAATTGGCTTCATAGTTTCACTGTCGTCTTGGCATCATCCAA
AACATCACCAAGATGAAACTGACGTGCATGATGATCGTTGCTGTGCTGTTCTTGACC
GCCTGGACATTGCCACGGCTGATGACTCCAGCAATGGATTGGAGAATCTTTTTTG
20 AAGGCACATCACGAAATGAACCCCGAAGCCTCTAAGTTGAACGAGAGGGTGCCTTGA
TGCTGGTGAAGTTGTGATATTTCACATGCTGCGGCTATTGCATTCTCTT
TTCTGCGCATAAAACTACCGTGATGTCTACTCCCCTCTGTGCTACCTGGCTTGAT
CTTGATTGGCGCGTACCCCTCACTGGTTATGAAACCCCTGATCCAGCTCTGGAG
GCCTCGGGGGTTAACATCCAAATAAGCGACA (SEQ ID NO:50)

Translation:

MKLTGMMIVAVLFLTAWTFATADDSSNGLENLFLKAHHEMNPEASKLNERCLDAGEV
CDIFFPTCCCGYCILLFCA (SEQ ID NO:51)

Toxin Sequence:

Cys-Leu-Asp-Ala-Gly-Xaa1-Val-Cys-Asp-Ile-Phe-Phe-Xaa3-Thr-Cys-Cys-Gly-Xaa5-Cys-Ile-
Leu-Leu-Phe-Cys-Ala-^ (SEQ ID NO:52)

3.5 **Name:** KK-1
Species: textile

Toxin Sequence:

Cys-Ile-Xaa1-Gln-Phe-Asp-Xaa3-Cys-Xaa1-Met-Ile-Arg-His-Thr-Cys-Cys-Val-Gly-Val-Cys-
10 Phe-Leu-Met-Ala-Cys-Ile-^ (SEQ ID NO:53)

3.5 **Name:** KK-2
Species: textile

Toxin Sequence:

Cys-Ala-Xaa3-Phe-Leu-His-Xaa3-Cys-Thr-Phe-Phe-Xaa3-Asn-Cys-Cys-Asn-Ser-Xaa5-

Cys-Val-Gln-Phe-Ile-Cys-Leu-[^] (SEQ ID NO:54)

5 **Name:** Om6.1
Species: omaria
Isolated: No
Cloned: Yes

10 **DNA Sequence:**
ATGAAACTGACGTGCATGATGATCGTTGCTGTGCTGTTCTGACCGCCTGGACATTG
GCCACGGCTGATGACCCCCAGAAATGGATTGGAGAATTTCGAAGACACAACA
CGAAATGAAGAACCCCGAAGCCTCTAAATTGAACAAGAGGTGCCTAGCAGAACATG
AAACTTGTAAATATTTACACAAAATGCTGCGAAGGCGTGTGCATTTATCTGCG
TACAAGCTCCAGAGTGATGTCTCTCCTCCCCTC (SEQ ID NO:55)

15 **Translation:**
MKLTCMMIVAVLFLTAWTFATADDPRNGLENFFSKTQHEMKNPEASKLNKRCLAEHE
TCNIFTQNCCEGVCIFICVQAPE (SEQ ID NO:56)

20 **Toxin Sequence:**
Cys-Leu-Ala-Xaa1-His-Xaa1-Thr-Cys-Asn-Ile-Phe-Thr-Gln-Asn-Cys-Cys-Xaa1-Gly-Val-Cys-
Ile-Phe-Ile-Cys-Val-Gln-Ala-Xaa3-Xaa1-[^] (SEQ ID NO:57)

25 **Name:** Om6.3
Species: omaria
Isolated: No
Cloned: Yes

30 **DNA Sequence:**
ATGAAACTGACTGTCATGATGATCGTTGCTGTGCTGTTCTGACCGCCTGGACATTG
GCCACGGCTGAAGACCCCCAGACATGGATTGGAGAATCTTTTCGAAGGCACATCA
CGAAATGAAGAACCCCTGAAGACTCTAAATTGGACAAGAGGTGCATTCCACATTTG
ACCCTTGTGACCCGATACGCCACACCTGCTGCTTGGCCTGTGCCTACTAATAGCCT
35 GCATCTAAAATGCCGTGATGTCTCTCCTCCCATC (SEQ ID NO:58)

35 **Translation:**
MKLTVMIVAVLFLTAWTFATAEDPRHGLENLFSKAHHEMKNPEDSKLDKRCIPHDFP
CDPIRHTCCFGLCLLIACI (SEQ ID NO:59)

40 **Toxin Sequence:**
Cys-Ile-Xaa3-His-Phe-Asp-Xaa3-Cys-Asp-Xaa3-Ile-Arg-His-Thr-Cys-Cys-Phe-Gly-Leu-Cys-
Leu-Leu-Ile-Ala-Cys-Ile-[^] (SEQ ID NO:60)

45 **Name:** Om6.4
Species: omaria

Isolated: No
Cloned: Yes

DNA Sequence:

5 ATGAAACTGACGTGCGTGATGACCGTTGCTGTGCTGTTCTTGACCGCCTGGACATTG
 GTCACGGCTGAAGACCCCAGAGATGGATTGAAGAAATCTTTATCAAATGCACATAA
 CGAAATGAAGAACCCCGAACGCCTCTACATTGAACGAGAGGTGCCTGGGTTGGTGAAGCTTGTCTTATACTTATTCA
 GACTGCTGCCTATTGCCTGGTGCATCTGCCTATAAAACTACCGTGATGTCTTCTCCTCCCCCTC (SEQ ID NO:61)

10

Translation:

MKLTCVMTAVLFLTAWTFVTAEDPRDGLKNLLSNAHNEMKNPEASTLNERCLGFGE
 ACLILYSDCCGYCVGAICL (SEQ ID NO:62)

15

Toxin Sequence:

Cys-Leu-Gly-Phe-Gly-Xaa1-Ala-Cys-Leu-Ile-Leu-Xaa5-Ser-Asp-Cys-Cys-Gly-Xaa5-Cys-Val-Gly-Ala-Ile-Cys-Leu-^ (SEQ ID NO:63)

20

Name: Au6.1
Species: aulicus
Isolated: No
Cloned: Yes

25

DNA Sequence:

ATGAAACTGACGTGATGATCGTTGCTGTGCTGTTCTTGACCGCCTGGACATTG
 GCCACGGCTGATGACCCCAGAAATGGATTGGAGAATCTTTTCGAAGACACAACA
 CAAAATGAAGAACCCCGAACGCCTCTAAATTGAACAAAGAGGTGCAAAGCAGAAAAT
 GAACTTGTAAATATATTATACAAAATGCTGCACGGGACGTGCCTCTTATCTGC
 30 ATACAAAATCCACAGTGATGTCTCTCCTACCCCTC (SEQ ID NO:64)

30

Translation:

MKLTCVMIVAVLFLTAWTFATADDPRNGLENLFSKTQHMKKNPEASKLNKRCKAENE
 LCNIFIQNCCDGTCLLICIQNPQ (SEQ ID NO:65)

35

Toxin Sequence:

Cys-Lys-Ala-Xaa1-Asn-Xaa1-Leu-Cys-Asn-Ile-Phe-Ile-Gln-Asn-Cys-Cys-Asp-Gly-Thr-Cys-Leu-Leu-Ile-Cys-Ile-Gln-Asn-Xaa3-Gln-^ (SEQ ID NO:66)

40

Name: Au6.2
Species: aulicus
Isolated: No
Cloned: Yes

45

DNA Sequence:

ATGAAACTGACGTGCGTGATGATCGTTGCTGTGCTGTTCTTGACCGCCTGGACATTG

GCCACGGCTGATGACCCCAGAAATGGATTGGATAATCGTTTCGAAGGCACGTCA
 CGAAATGAATAACCGCAGAGCCTCTAAATTGAACAAGAGGTGCCTGAGTTGGTG
 AACTTTGTAATTTTTCCCACCTGCTGCGCTATTGCGTTCTCTGTCTGCCTA
 TAAACTACCGTGATGTCTCTCTCCCCTC (SEQ ID NO:67)

5

Translation:

MKLTCVMIVAVLFLTAWTFATADDPRNLDNRFSKARHEMNNRASKLNKRCLEFGE
 LCNFFFPTCCGYCVLLVCL (SEQ ID NO:68)

10

Toxin Sequence:

Cys-Leu-Xaa1-Phe-Gly-Xaa1-Leu-Cys-Asn-Phe-Phe-Xaa3-Thr-Cys-Cys-Gly-Xaa5-Cys-
 Val-Leu-Leu-Val-Cys-Leu-^ (SEQ ID NO:69)

15

Name: Da6.5
Species: dalli
Isolated: No
Cloned: Yes

20

DNA Sequence:

ATGAAACTGACGTGTGATGATCGTTGCTGTGCTGTTCTGACCGCCTGGACATTT
 GTCATGGCTGATGACTCCGGAAATGGATTGGAAAATCTGTTTCGAAGGCACATCA
 CGAAATGAAGAACCCCTGAAGCCTCTAAATTGAACAAGAGGTGCCTCAAAGCAGTG
 AATTATGTGATGCGCTGGACTCAGACTGCTGCAGTGGTGTTCATGGTATTTCT
 GCCTATAAAACTGCCGTGATGTCTTCTATCCCCTC (SEQ ID NO:70)

25

Translation:

MKLTCVMIVAVLFLTAWTFVMADDSGNGLENLFSKAHHEMKNPEASKLNKRCQAQSSE
 LCDALDSDCCSGVCMVFFCL (SEQ ID NO:71)

30

Toxin Sequence:

Cys-Ala-Gln-Ser-Ser-Xaa1-Leu-Cys-Asp-Ala-Leu-Asp-Ser-Asp-Cys-Ser-Gly-Val-Cys-
 Met-Val-Phe-Phe-Cys-Leu-^ (SEQ ID NO:72)

35

Name: Di6.4
Species: distans
Isolated: No
Cloned: Yes

40

DNA Sequence:

ATGAAACTGACGTGCGTGATGACCGTTGCTGTGCTGTTCTGACCGCCIGGACATTC
 GTCACGGCTGAAGACCCCAGAGATGGATTGAGGAATCTTTATCGAATGCACGTCA
 TGAAATGAAGAACCCCGAAGCCTCTAAATTGAACGAGAGGTGCCTGGGTTGGTG
 AAGCTTGTCTTATGCTTATTCAAGACTGCTGCAGCTATTGCGTTGGTGTCTGCCT
 ATAAAACCTACCGTGATGTCTTACTCCCATC (SEQ ID NO:73)

Translation:

MKLTCVMTAVLFLTAWTFVTAEDPRDGLRNLLSNARHEMKNPEASKLNERCLGFGE
ACLMLYSDCCSYCVGAVCL (SEQ ID NO:74)

5 **Toxin Sequence:**

Cys-Leu-Gly-Phe-Gly-Xaa1-Ala-Cys-Leu-Met-Leu-Xaa5-Ser-Asp-Cys-Cys-Ser-Xaa5-Cys-Val-Gly-Ala-Val-Cys-Leu-^ (SEQ ID NO:75)

10 **Name:** Pn6.2
Species: pennaceus
Isolated: No
Cloned: Yes

15 **DNA Sequence:**

ATGAAACTGACGTGCCTGATGACCGTTGCTGTGCTGTTCTTGACCGCCTGGACATT
GCCACGGCTGAAGACCCCAGAAATGGATTGGAGAATCTTTTTCGAAGGCACATCA
CGAAATGAAGAACCCCTGAAGACTCTAAATTGGACAAGAGGTGCGTAAATATCTTG
20 ACCCTTGTGACATGTTACGCCACACCTGCTGCTTGGCCTGTGCGTACTAATAGCCT
GCATCTAAAATGCCGTGATGTCTTACTCCCATC (SEQ ID NO:76)

Translation:

25 MKLTCLMTAVLFLTAWTFATAEDPRNGLENLFSKAHHEMKNPEDSKLDKRCVKYLD
PCDMLRHTCCFGLCVLIACI (SEQ ID NO:77)

Toxin Sequence:

30 Cys-Val-Lys-Xaa5-Leu-Asp-Xaa3-Cys-Asp-Met-Leu-Arg-His-Thr-Cys-Cys-Phe-Gly-Leu-Cys-Val-Leu-Ile-Ala-Cys-Ile-^ (SEQ ID NO:78)

35 **Name:** Pn6.3
Species: pennaceus
Isolated: No
Cloned: Yes

DNA Sequence:

40 ATGAAACTGACGTGTGATGATCGTTGCTGTGCTGTTCTTGACCGCCTGGACATT
GCCACGGCTGATGACCCCAGAAATGGATTGGGAATCTTTTTCGAATGCACATCAC
GAAATGAAGAACCCCGAAGCTTCTAAATTGAACGAGAGGTGCCTTGGTTGGTGA
AGTTTGCAATTCTTTTCAAACGTGCAGCTATTGCGTTGCTCTTGTCTGCC
45 TAAAACCTACCGTGATGTCTTCTATTCCCCCTC (SEQ ID NO:79)

Translation:

MKLTCVMIVAVLFLTAWTFATADDPRNGLGNLFSAHHHEMKNPEASKLNERCLGFGE
VCNFFFNCCSYCVALVCL (SEQ ID NO:80)

5 **Toxin Sequence:**

Cys-Leu-Gly-Phe-Gly-Xaa1-Val-Cys-Asn-Phe-Phe-Phe-Xaa3-Asn-Cys-Cys-Ser-Xaa5-Cys-Val-
Ala-Leu-Val-Cys-Leu-^ (SEQ ID NO:81)

10 **Name:** Pn6.4
Species: pennaceus
Isolated: No
Cloned: Yes

15 **DNA Sequence:**

ATGAAACTGACGTGCGTGATGCTCGTTGCTGTGCTGTTCTTGACCGCCTGGACATTG
GCCACGGCTGATGACTCCAGCAATGGACTGGAGAATCTTTTTCGAAGGCACATCA
20 CGAAATGAAGAACCCCGAAGCCTCTAAATTGAACAAGAGGTGCATTCCACAATTG
ATCCTTGACATGGTACGTACACTTGCTGCAAAGGGTTGTGCGTACTAATAGCCT
GCTCTAAAATGCGTGATGTCTTCATCTCCCTC (SEQ ID NO:82)

25 **Translation:**

MKLTCVMLVAVLFLTAWTFATADDSSNGLENLFSKAHHEMKNPEASKLNKRCIPQFDP
CDMVRHTCCKGLCVLIACSKTA (SEQ ID NO:83)

30 **Toxin Sequence:**

Cys-Ile-Xaa3-Gln-Phe-Asp-Xaa3-Cys-Asp-Met-Val-Arg-His-Thr-Cys-Cys-Lys-Gly-Leu-Cys-
Val-Leu-Ile-Ala-Cys-Ser-Lys-Thr-Ala-^ (SEQ ID NO:84)

35 **Name:** Pn6.7
Species: pennaceus
Isolated: No
Cloned: Yes

40 **DNA Sequence:**

ATGAAACTGACGTGCTTGATGATCGTTGCTGTGCTGTTCTTGACCGCCTGGACATTG
GCCACGGCTGATGACCCAGAAATGGATTGGAGAATTTTTTCGAAGACACAACA
CGAAATGAAGAACCCCGAAGCCTCTAAATTGAACAAGAGGTGCAAAGCAGAAAGT
45 GAAGCTTGTAAATATAATTACACAAAACCTGCTGCGACGGCAAGTGCCTTTTCTGC
ATACAAATTCCAGAGTGATGTCTTCCTCCATC (SEQ ID NO:85)

Translation:

MKLTCLMIVAVLFLTAWTFATADDPRNGLENFFSKTQHEMKNPEASKLNKRCKAESEA
CNIITQNCCDGKCLFFCIQIPE (SEQ ID NO:86)

5

Toxin Sequence:

Cys-Lys-Ala-Xaa1-Ser-Xaa1-Ala-Cys-Asn-Ile-Ile-Thr-Gln-Asn-Cys-Cys-Asp-Gly-Lys-Cys-
Leu-Phe-Phe-Cys-Ile-Gln-Ile-Xaa3-Xaa1-^ (SEQ ID NO:87)

10

Name: Omaria3
Species: omaria
Isolated: No
Cloned: Yes

15

DNA Sequence:

GGTCGACATCATCATCATCATCGATCCATCTGCCATCCATTCAATTGCTCGCT
GCCAGACTGTCATAAATATTGAGTCTCTCCTCTGTTGTATCTGACAGATTGAAC
AAGAGGTGCATTGACGGTGGTGAATTGATATTGTTTCAAAGTGCAGT
GGGTGGTGCATTATTCTCGTCTCGCATGAAACTACCGTGATGCTTCTACTCCCC
TAGTAGTAGTAGGCGGGCGCTCTAGAGGATCCAAGCTACGTACCGTGCATGCGA
CGTCATAGCTCTTCTATAGTGTACCTAAATTCAATTCACTGGCCGTCGTTTACAAC
GTCGTGACTGGAAAACCCTGGCGTTACCCAACTTAATGCCCTGCAGCACATCCCC
CTTCGCCAGCTGGCGTAATAGCGAAGAGGCCGCACCGATGCCCTCCAACAGT
TTGCGCAGCCTGAATGGCGAATGGGACGCGCCCTGTAGCGGCGCATTAAGCGCGGC
GGGTGGTGGTGGGTaCGCGCAGCGTGACCGGTACACTGCCAGCGCCCTAGCGCCCGC
TCCTTTGCTTCTCCCTTCTGCCACCGTTCCgCCCAGGGTTTCCCCTCaAG
30 CTC (SEQ ID NO:88)

20

25

Translation:

LNKRCIDGGEICDIFPNCCSGWCIILVCA (SEQ ID NO:89)

35

Toxin Sequence:

Cys-Ile-Asp-Gly-Gly-Xaa1-Ile-Cys-Asp-Ile-Phe-Phe-Xaa3-Asn-Cys-Cys-Ser-Gly-Xaa4-Cys-
Ile-Ile-Leu-Val-Cys-Ala-^ (SEQ ID NO:90)

40

45

Name: Omaria1
Species: omaria
Isolated: No
Cloned: Yes

DNA Sequence:

GGTCGACATCATCATCATCGATCCATCTGTCCATCCATCCATTCAATTGCTGCC
 5 AGACTGTCATAAAATATTGAGTCTCTCCTCTGTTGTATCTGACAGATTGAACAAG
 AGGTGCCTTGACGGTGGTGAAAATTGTTGTTCCAAGCTGCTGCAGTGGG
 10 TGGTGCATTGTTCTCGTCTGCGATGAAACTACCGTGATGTCTTACTCCCCCTAG
 TAGTAGTAGGCGGCCGCTCTAGAGGATCCAAGCTTACGTACGCGTGCATGCGACGT
 CATAGCTCTTCTATAGTGTACCTAAATTCAATTCACTGGCCGTCGTTACAACGTC
 GTGACTGGGAAAACCCTGGCGTACCCAACTTAATCGCCTTGACGCACATCCCCCTT
 TCGCCAGCTGGCGTAATAGCGAAGAGGCCCCGACCGATGCCCTCCAAACAAGTT
 15 GCGCAGCCTGAATGGCGAATGGGACGCGCCCTGTAGCGGCGCATTAGCGCGGCCGG
 GTGTGGTGGTTACGCGCACCGTACCGCTACACTGCCAGCGCCCTAGCCGCCGCT
 CCTTCGCTTCTTCCCTTcCTTCTCGCACGTTGGCCGGCTTCCCCGTCAAGCTCT
 AAATCGGGGGCTTCCCTTTA (SEQ ID NO:91)

15 **Translation:**

LNKRCLDGGEICGILFPSCCSGWCIVLVCA (SEQ ID NO:92)

20 **Toxin Sequence:**

Cys-Leu-Asp-Gly-Gly-Xaa1-Ile-Cys-Gly-Ile-Leu-Phe-Xaa3-Ser-Cys-Cys-Ser-Gly-Xaa4-Cys-
 Ile-Val-Leu-Val-Cys-Ala-^ (SEQ ID NO:93)

25 **Name:** Marm7
Species: marmoreus
Isolated: No
Cloned: Yes

30 **DNA Sequence:**

GGTCGACATCATCATCATCGATCCATCTGTCCATCCATCCATTCAATTGCTGCC
 AGACTGTAATAAAATATTGAGTCTCTCTTCTGTTGTATCTGACAGATTGAACAAG
 AGGTGCCTTGAGTTGGTGAAGTTGTAATTTTTCCAAACCTGCTGCAGGCTATT
 35 GCGTTCTTCTGTCTGCCTATAAAACTACCGTGATGTCTTACTCCCCCTAGTAGT
 AGTAGGCGGCCGCTCTAGAGGATCCAAGCTTACGTACGCGTGCATGCGACGTCATA
 GCTCTTCTATAGTGTACCTAAATTCAATTCACTGGCCGTCGTTACAACGTCGTGA
 CTGGGAAAACCCTGGCGTACCCAACTTAATCGCCTTGACGCACATCCCCCTTCGC
 40 CAGCTGGCGTAATAGCGAAGAGGCCCCGACCGATGCCCTCCAAACAGTIGCGCA
 GCCTGAATGGCGAATGGGACGCGCCCTGTAGCGGCGCATTAGCGCGGGGTGTG
 GTGGTTACGCGCAGCGTACCGCTACACTTGCAGCGCCCTAGCGCCCGCTCCTTCG
 CTTTCTCCCTTCTCGCACGTTGCCAGGGCTTCCCCGTCAA (SEQ ID NO:94)

45 **Translation:**

LNKRCLEFGEVCNFFFPTCCGYCVLLVCL (SEQ ID NO:95)

Toxin Sequence:

Cys-Leu-Xaa1-Phe-Gly-Xaa1-Val-Cys-Asn-Phe-Phe-Phe-Xaa3-Thr-Cys-Cys-Gly-Xaa5-Cys-
Val-Leu-Leu-Val-Cys-Leu-[^] (SEQ ID NO:96)

5

Name: Marm12
Species: marmoreus
Isolated: No
Cloned: Yes

10

DNA Sequence:

GAAAGCTGGTACGCCTGCAGGTACCGGTCCCGAATTCCCGGGTCGACATCATC
 15 ATCATCGATCCATCTGTCCATCCATTCAATTCAATTGCTGCCAGACTGTAATAA
 ATATTGAGTTCTCCTCTGTTGTATCTGACAGGTTGAACAAAGAGGTGCCAAGAG
 TTCGGTGAAGTTGTAAATTTTTCCCAGACTGCTGCCATTGCGTTCTTTAC
 TCTGCATATAAAACTACCGTGATGTCTCTTCCCATTAGTAGTAGTAGTAG
 TAGGCAGGCCGCTCTAGAGGATCCAAGCTTACGTACCGGTGCATGCGACGT
 20 TACTGCATAGTCACCTAAATTCAATTCACTGGCCGTCGTTTACAACCGTCGTGAC
 TGGGAAAACCCCTGGCGTTCCCAACTTAATTGCCTTGCAGCACAT (SEQ ID NO:97)

20

Translation:

25 LNKRCQEFGEVCNFFFDPCCGYCVLLCI (SEQ ID NO:98)

25

Toxin Sequence:

Cys-Gln-Xaa1-Phe-Gly-Xaa1-Val-Cys-Asn-Phe-Phe-Phe-Xaa3-Asp-Cys-Cys-Gly-Xaa5-Cys-
 30 Val-Leu-Leu-Leu-Cys-Ile-[^] (SEQ ID NO:99)

30

Name: Omaria7
Species: omaria
Isolated: No
Cloned: Yes

35

DNA Sequence:

40 TTTGAAGCNGGTACGCCTGCAGGTACCGGTCCCGAATTCCCGGGTCGACATCATCA
 TCATCATCGATCCATCTGTCCATCCATTCAATTGCTACCGAGACTGTAATA
 AATATTGCGGTCTCTCTTGTATCTGACAGATTGGACAAGAGGTGCATTCC
 ACATTTGACCCCTTGTGACCCGATACGCCACACCTGCTGCTTGGCCTGTGCCTACT
 AATAGCCTGCATCTAAACTGCCGTATGTCTCTCCCTCTAGTAGTAGTAGG
 45 CGGCCGCTCTAGAGGATCCAACCTTACGTACCGGTGCATGCGACGT
 TATAGTGTACCTAAATTCAATTCACTGGCCGTCGTTACAACGTCGTGACTGGGA
 AAACCCCTGGCGTTACCCAACCTTAATGCCTTGCAGCACATCCCCCTTCGCCAGCTG

45

GCGTAATAGCGAAGAGGCCGCACCGATGCCCTCCAACAGTTGCGCAGCCTGA
ATGGCGAATGGGACGCGCCCTGTAGCGGCGCT (SEQ ID NO:100)

Translation:

5 LDKRCIPHFDPCDPIRHTCCFGLLLIACI (SEQ ID NO:101)

Toxin Sequence:

10 Cys-Ile-Xaa3-His-Phe-Asp-Xaa3-Cys-Asp-Xaa3-Ile-Arg-His-Thr-Cys-Cys-Phe-Gly-Leu-Cys-
Leu-Leu-Ile-Ala-Cys-Ile-[^] (SEQ ID NO:102)

15 **Name:** Omaria11
Species: omaria
Isolated: No
Cloned: Yes

20 **DNA Sequence:**

25 GGTACGCCCTGCAGGTACCGGTCCCGAATTCCCGGGTCGACATCATCATCATCGATCC
ATCTGTCCATCCATCCATTCTTCATTGCTGCCAGACTGTAATAATATTGAGTCT
CTCTTCTGTTGTATCTGACAGATTGAAACAAGAGGTGCCTTGAGTTGGTGAAGTT
TGTAAATTCCCCAACCTGCTGCGGCTATTGCGTTCTTGTCTGCCTATAAA
30 ACTACCGTGATGTCTTCTCTTCCCCTCTAGTAGTAGTAGAGCGGGCCGCTAGAGGAT
CCAAGCTTACGTACGCGTGCATGCGACGTAGCTCTCTATAGTGTACCTAAAT
TCAATTCACTGGCGTGTACACGCTGACTGGGAAACCCCTGGCGTTACCC
AACTTAATGCCCTGCAGCACATCCCCCTTCGCCAGCTGGCGTAATAGCGAAGAGG
CCCGCACCGATGCCCTCCAAACAGTTGCGCAGCCTGAATGGCGAATGGGACGCG
CCCTGTAGCGGCGCATTAAG (SEQ ID NO:103)

Translation:

35 LNKRCLEFGEVCNFFFPTCCGYCVLLVCL (SEQ ID NO:104)

Toxin Sequence:

40 Cys-Leu-Xaa1-Phe-Gly-Xaa1-Val-Cys-Asn-Phe-Phe-Phe-Xaa3-Thr-Cys-Cys-Gly-Xaa5-Cys-
Val-Leu-Leu-Val-Cys-Leu-[^] (SEQ ID NO:105)

45 **Name:** O6.5
Species: obscurus
Isolated: No
Cloned: Yes

DNA Sequence:

cgatccatctgtccatccatccatcggtcgctgccaactgtataataaccgagtctctgttttatctgacagATCGAAAA
 AGCAATGCCGTCAAAATGGTGAAGTGTGTATGCGAATTGGCACACTGCTGCAGT
 GGCCGTGTTCTCTGTCTAAACCAGCCGTATGTCTTACTCCCCTC (SEQ

5 ID NO:106)

Translation:

VSDRSKKQCRQNGEVCDANLAHCCSGPCFLFCLNQP (SEQ ID NO:107)

10 **Toxin Sequence:**

Ser-Lys-Lys-Gln-Cys-Arg-Gln-Asn-Gly-Xaa1-Val-Cys-Asp-Ala-Asn-Leu-Ala-His-Cys-Cys-
 Ser-Gly-Xaa3-Cys-Phe-Leu-Phe-Cys-Leu-Asn-Gln-Xaa3-^ (SEQ ID NO:108)

15
 Name: Af6.8
 Species: ammiralis
 Isolated: No
 20 Cloned: Yes

DNA Sequence:

ATGAAACTGACGTGCGTGATGATCATTGCTGTGCTGTTCTTGACCGCCTGGACATT
 25 GCCACGGCTGATGACTCCGGAAATGGATTGGAAAATCTTTTCGAAGGCACATCA
 CGAAATGAAGAACCCCAAAGCCTCTAAATTGAACAAGAGGTGCACTCAAAGCGGTG
 AACTTTGTGATGTGATAGACCCAGACTGCTGCAATAATTTCGATTATATTTCTG
 CATATAAAACTGCCGTGATGTCTTACTCCCCTC (SEQ ID NO:109)

30 **Translation:**

MKLTCVMIIAVLFLTAWTFATADDNGLENLFSKAHHEMKNPKASKLNKRCTQSHEL
 CDVIDPDCCNNFCIIFFCI (SEQ ID NO:110)

35 **Toxin Sequence:**

Cys-Thr-Gln-Ser-Gly-Xaa1-Leu-Cys-Asp-Val-Ile-Asp-Xaa3-Asp-Cys-Cys-Asn-Asn-Phe-Cys-
 Ile-Ile-Phe-Phe-Cys-Ile-^ (SEQ ID NO:111)

40
 Name: KK-2A
 Species: textile
 Isolated: No
 45 Cloned: Yes

DNA Sequence:

5 GGCATTACCTAAAACATCACCAAAATGAAACTGACGTGCATGATGATCGTTGCTGT
 GCTGTTCTGACCGCCTGGACATTGCCACGGCTGATGACTCCGGAAATGGATTGGA
 GAAACTTTTCGAATGCACATCACGAAATGAAGAACCCGAAGCCTCTAATTGA
 ACAAGAGGTGCGCTCCTTCTCACCTTGACCTTTCTCCAAACTGCTGCAA
 CGGCTATTGCCTCAATTATCTGCCTATAAAACTACTGTGATGTCTTCTATTCCCT
 C (SEQ ID NO:112)

Translation:

10 MKLTCMMIVAVLFLTAWTFATADDSGNGLEKLFSNAHHEMKNPEASNLNKRCAPFLH
 LCTFFFNCCNGYCVQFICL (SEQ ID NO:113)

Toxin Sequence:

15 Cys-Ala-Xaa3-Phe-Leu-His-Leu-Cys-Thr-Phe-Phe-Phe-Xaa3-Asn-Cys-Cys-Asn-Gly-Xaa5-Cys-
 Val-Gln-Phe-Ile-Cys-Leu-^ (SEQ ID NO:114)

20 **Name:** KKM1
Species: marmoreus
Isolated: No
Cloned: Yes

DNA Sequence:

25 GGATCCTAGCACAGTGAATTGGCTTACAGTTCCACTGTCGTCTTGGCATCATC
 CAAAACATCACCAAGATGAAACTGACGTGCATGATCGTTGCTGTGCTTCTTG
 ACCGCCTGGACATTGCCACGGCTGATGACCCAGAAATGGATTGGAGAAATCTTTT
 TCGAAGGCACATCACGAAATGAAGAACCCAAAGACTCTAAATTGAACAAGAGGT
 30 GCCTTGACGCTGGTGAAATGTGATCTTTAATTCAAAATGCTGCAGTGGGTGGT
 GCATTATTCTCTTCTGCGCATAAAACTACCGTGATGTCTTCACTCCCTCTGTGCTA
 CCTGGCTTGATCTTGATTGGCGGTGCCCTCACTGGTTATGAACCCCCCTGATCC
 GACTCTCTGGCGGCCTCGGGGGTTAACATCCAAATAAGCCGACACGATACTGAC
 GTAGAAAAAAAAAAAAAAAAAAAAA (SEQ ID NO:115)

35 **Translation:**

MKLTCMMIVAVLFLTAWTFATADDPRNGLENLFSKAHHEMKNPKDSKLNKRCLDAGE
 MCDLFNSKCCSGWCIILFCA (SEQ ID NO:116)

40 **Toxin Sequence:**

Cys-Leu-Asp-Ala-Gly-Xaa1-Met-Cys-Asp-Leu-Phe-Asn-Ser-Lys-Cys-Cys-Ser-Gly-Xaa4-Cys-
 Ile-Ile-Leu-Phe-Cys-Ala-^ (SEQ ID NO:117)

45

Name: KKM4
Species: marmoreus
Isolated: No
Cloned: Yes

5

DNA Sequence:

10 GCCGAAAACATCACCAAGATGAAACTGACGAGCATGATGATCGTGCTGTGCTGTT
 CTTGACCGCCTGGACATTCGTACGGCTGACGACTCCGGAAATGGATTGGAGAAC
 TTTTTCGAAGGCACATCACGAGATGAAGAACCCCAAAGACTCTAAATTGAACAAG
 AGGTGCCTTGACGGTGGTGAAATTGTTGTTCAAGCTGCTGCAGTGGG
 TGGTGCATTGTTCTCGTCTGCATGAAACTACCGTGATGTCTACTCCCCTCTGT
 GCTACCTGGCTTGATCTTGATTGGCGCGTGCCTCACTGGTTATGAACCCCCCTG
 15 ATCCGACTCTCTGGCGCCTGGGGGTTAACATCAAATAAGCGACACGACAAT
 GACAAAAAAAAAAAAAAAAAAAAA (SEQ ID NO:118)

Translation:

20 MKLTSMMIVAVLFLTAWTFVTADDNGLENLFSKAHHEMKNPKDSKLNKRCLDGGE
 ICGILFPSCSGWCIVLVCA (SEQ ID NO:119)

Toxin Sequence:

25 Cys-Leu-Asp-Gly-Gly-Xaa1-Ile-Cys-Gly-Ile-Leu-Phe-Xaa3-Ser-Cys-Cys-Ser-Gly-Xaa4-Cys-
 Ile-Val-Leu-Val-Cys-Ala-^ (SEQ ID NO:120)

30 **Name:** KKM5
Species: marmoreus
Isolated: No
Cloned: Yes

DNA Sequence:

35 GCTAGCACAGTGAATTGGCTTACAGTTTCACTGTCGTCTTGGCATCATCAA
 AACATCACCAAGATGAAACTGACGTGCATGATGATCGAAGCAGAGCTGTTCTGAC
 CGCCTGGACATTGCCACGGCTGATGACCCAGAAATGGATTGGAGAAC
 40 GAAGGCACATCACGAAATGAAGAACCCGAAGCCTCTAAATTGAACAAGAGGTGC
 CCTAACACTGGTGAATTATGTGATGTGGTTAACAAAACGCTGCTATACCTATTGC
 TTTATTGTAGTCTGCCCTATATAACTACCGTGATGTCTACTCCCCTGTGCTGC
 CTGGCTTGATCTTGATTGGCGCGTGCCTCACTGGTTATGAACCCCCCTGATCCG
 ACTCTCTTGCGGCCTCAGGGGTTAACATCAAATAAGCGACACGAAAATGAAAA
 AAAAAAAAAAAAAAAA (SEQ ID NO:121)

Translation:

MKLT CMMIEAELFLTAWTFATADDPRNGLENLFSKAHHEMKNPEASKLNKRCPTGEL

CDVVEQNCCYTYCFIVVCPI (SEQ ID NO:122)

Toxin Sequence:

5 Cys-Xaa3-Asn-Thr-Gly-Xaa1-Leu-Cys-Asp-Val-Val-Xaa1-Gln-Asn-Cys-Cys-Xaa5-Thr-Xaa5-
Cys-Phe-Ile-Val-Val-Cys-Xaa3-Ile-^ (SEQ ID NO:123)

10 **Name:** KKM6
Species: marmoreus
Isolated: No
Cloned: Yes

DNA Sequence:

15 TTGCACGGTGAATTGCTTATATTTTCTACTGTCGTCTTGGCATCATCCAAAACA
TCACCAAGATGAAACTGACGTGCATGATGATCGTGTGCTGTGCTTGCCTGACCGCCT
GGACATTGTCACGGCTGTGCCTCACTCCAGCGATGTATTGGAGAATCTTATCTGA
AGGCACCTCACGAAACGGAAAACCACGAAGCCTCTAAATTGAACGTGAGAGACGA
20 CGAGTGCACCTCCTGGAGATTTGTGGCTTTAAAATTGGGCCGCTGCTG
CAGTGGCTGGTGCCTCCTGGTGCCTAAACTGCCGTGATGTCTCTATTCCCCT
CTGTGCTACCTGGCTTGATCTTGATTGGCGCGTGCCTTCAGTGGTTATGAACCCCC
CTGATCCGACTCTCTGGGGCCTCGGGGGTTCAACATCCAAATAAAGCTGACAACA
CAATAAAAAAAA (SEQ ID NO:124)

25 **Translation:**

30 MKLTCMMIVAVLFLTAWTFVTAVPHSSDVLENLYLKALHETENHEASKLNRDDECEP
PGDFCGFFKIGPPCCSGWCFLWCA (SEQ ID NO:125)

Toxin Sequence:

35 Asp-Asp-Xaa1-Cys-Xaa1-Xaa3-Xaa3-Gly-Asp-Phe-Cys-Gly-Phe-Phe-Lys-Ile-Gly-Xaa3-Xaa3-
Cys-Cys-Ser-Gly-Xaa4-Cys-Phe-Leu-Xaa4-Cys-Ala-^ (SEQ ID NO:126)

40 **Name:** C. striatus S2
Species: striatus
Isolated: No
Cloned: Yes

DNA Sequence:

45 ATGAAACTGACGTGTGATGATCGTTGCTGTGCTTGCCTGACCGCCTGGACATTG
GTCACGGCTGTGCCTCACTCCAGCGATGATTGGAGAATCTTATCTGAAGGCACCT
CACGAAACGGAAAACCACGAAGCCTCTAAATTGAACGTGAGAGACGACGAGTGCG
AACCTCCTGGAGATTTGTGGCTTTAAAATTGGGCCGCTGCTGCAGTGGCT

GGTGCTTCCTCTGGTGCGCATAAAACTGCCGTATGTCTTCTCCTCCCTC (SEQ ID NO:127)

Translation:

MKLTCVMIVAVLFLTAWTFVTAVPHSSDALENLYLKALHETENHEASKLNVRDDECEP
PGDFCGFFKIGPPCCSGWCFLWCA (SEQ ID NO:128)

Toxin Sequence:

Asp-Asp-Xaa1-Cys-Xaa1-Xaa3-Xaa3-Gly-Asp-Phe-Cys-Gly-Phe-Phe-Lys-Ile-Gly-Xaa3-Xaa3-Cys-Cys-Ser-Gly-Xaa4-Cys-Phe-Leu-Xaa4-Cys-Ala-[^] (SEQ ID NO:129)

1.5 **Name:** Om6.5
Species: omaria
Isolated: No
Cloned: Yes

20 **DNA Sequence:**

ATGAAACTGACGTGCGTGATGATCGTTGCTGTGCTGTTCTGACCGCCTGGACATTGTCACGGCTGTGCCTCACTCCAGCAATGCATTGGAAAATCTTATCTGAAGGCACGTCACGAAATGGAAAACCCCGAAGCCTCTAAATTGAACACGAGAGACGACGATTGCGAACCTCCTGGAAATTTTGTGGCATGATAAAAATTGGGCCGCCTGCTGCAGTGGCTGGTCTTTTCGCCTGCGCCTAAACTGCCGTATGTCTCCTCCCTC (SEQ ID NO:130)

Translation:

MKLTCVMIVAVLFLTAWTFVTAVPHSSNALENLYLKARHEMENPEASKLNTRDDDCEP
PGNFCGMIKIGPPCCSGWCFFACA (SEQ ID NO:131)

Toxin Sequence:

Asp-Asp-Asp-Cys-Xaa1-Xaa3-Xaa3-Gly-Asn-Phe-Cys-Gly-Met-Ile-Lys-Ile-Gly-Xaa3-Xaa3-Cys-Cys-Ser-Gly-Xaa4-Cys-Phe-Phe-Ala-Cys-Ala-[^] (SEQ ID NO:132)

10 **Name:** Au6.3
Species: aulicus
Isolated: No
Cloned: Yes

15 **DNA Sequence:**

ATGAAACTGACGTGCCTGATGATAGTGCTGTGCTGTTCTGACCGCCTGGACATTG

GTCACGGCTGTGCCTCACTCCAGCAATGCATTGGAGAACATCTTATCTGAAGGCACGT
 CACGAAATGGAAAACCCCGAACGCCTCTAAATTGAACACGAGAGACTACGATTGCGA
 ACCTCCTGGAAATTTGTGGCATGATAAAAATTGGGCCCTGCTGCAGTGGCTG
 GTGCTTTTCGCCTGCGCCTAAAACGTCCGTATGTCTCCTCCCTC (SEQ ID

5 NO:133)

Translation:

10 MKLTCLMIVAVLFLTAWTFVTAVPHSSNALENLYLKARHEMENPEASKLNTRDYDCEP
 PGNFCGMIKIGPPCCSGWCFAC (SEQ ID NO:134)

Toxin Sequence:

15 Asp-Xaa5-Asp-Cys-Xaa1-Xaa3-Xaa3-Gly-Asn-Phe-Cys-Gly-Met-Ile-Lys-Ile-Gly-Xaa3-Xaa3-
 Cys-Cys-Ser-Gly-Xaa4-Cys-Phe-Phe-Ala-Cys-Ala-^ (SEQ ID NO:135)

20 **Name:** Marm9
Species: marmoreus
Isolated: No
Cloned: Yes

DNA Sequence:

25 GGTCGACATCATCATCATCGATCCATCTGTCCATCCATCTATTCAATTCAATTCTG
 GCCAAACTGTAATAAATAATGCAAGTCTCTCTTCTGTTGTATCTGACAGATTGAA
 CACGAGAGACGACGATTGCGAACCTCTGGAAATTGGCATGATAAAAATTG
 GGCGCCTTGCTGCAGTGGCTGGTCTTTCGCCCTGCCCTAAACTGCCGTGATG
 TCTTCTCTCCCTCTAGTAGTAGTAGGGCGGCCCTAGAGGATCCAAGCTTACGT
 30 ACGCGTGCATGCGACGTCATAGCTCTTCTATAGTGTACCTAAATTCAATTCAATTG
 CCGTCGTTTACAACGTCGTGACTGGAAAACCTGGCGTTACCCAACTTAATGCC
 TTGCAGCACATCCCCCTTCGCCAGCTGGCGTAATAGCGAAGAGGCCCGCACC
 CGCCCTCCCAACAGTTGCGCAGCCTGAATGGGAATGGGACGCCCTGTAGCG
 CGCATTAAAGCGCGGGTGTGGTGGTTACGCCAGCCGTGACCCGCTACACTG
 35 CCAGCGCCCTAGCGCCGCTCCTTCGCTTCTCCTTCTGCCACGTTGCC
 GGCTTTCCCGTCAAGCTAAATGGGGCTCCTTAGGGTCCGATTAAAGTGCTT
 TAC (SEQ ID NO:136)

Translation:

40 LNTRDDDCEPPGNFCGMIKIGPPCCSGWCFAC (SEQ ID NO:137)

Toxin Sequence:

45 Asp-Asp-Asp-Cys-Xaa1-Xaa3-Xaa3-Gly-Asn-Phe-Cys-Gly-Met-Ile-Lys-Ile-Gly-Xaa3-Xaa3-
 Cys-Cys-Ser-Gly-Xaa4-Cys-Phe-Phe-Ala-Cys-Ala-^ (SEQ ID NO:138)

5 **Name:** Rg6.4
Species: regius
Isolated: No
Cloned: Yes

DNA Sequence:

10 TTGAACCAGAGAGACTGCCTTAGTAAAAACGCTTCTGTGCCTGGCCGATACTTGGACCACTGTGCTGCAGTGGCTGGTCTATACGTCTGCATGTAAAACGTGCCGTGATGTC TTCTATCCCCTC (SEQ ID NO:139)

Translation:

15 LNQRDCLSNAFCAWPLGPLCCSGWCLYVCM (SEQ ID NO:140)

Toxin Sequence:

20 Asp-Cys-Leu-Ser-Lys-Asn-Ala-Phe-Cys-Ala-Xaa4-Xaa3-Ile-Leu-Gly-Xaa3-Leu-Cys-Cys-Ser-Gly-Xaa4-Cys-Leu-Xaa5-Val-Cys-Met-^ (SEQ ID NO:141)

25 **Name:** R6.5
Species: radiatus
Isolated: No
Cloned: Yes

DNA Sequence:

30 ATTGAACAAGAAAGGTGATGACTGCCTTGCTGTTAAAAAAAATTGTGGCTTCCAA AACTTGGAGGGCCATGCTGCAGTGGCTGTGCTTTCTGCGCCTAAAACGTGCC GTGATGTCTTCTCCTCCCCT (SEQ ID NO:142)

Translation:

LNKKGDDCLAVKKNCFPKLGPGCCSGLCFFVCA (SEQ ID NO:143)

Toxin Sequence:

40 Gly-Asp-Asp-Cys-Leu-Ala-Val-Lys-Lys-Asn-Cys-Gly-Phe-Xaa3-Lys-Leu-Gly-Gly-Xaa3-Cys-Cys-Ser-Gly-Leu-Cys-Phe-Phe-Val-Cys-Ala-^ (SEQ ID NO:144)

45 **Name:** Rg6.2
Species: regius
Isolated: No

Cloned: Yes

DNA Sequence:

5 TTGAATCAGAGCGACTGCCTCCTAGAGACACATTCTGTGCCTGCCGCAACTTGGAC
CTACTGTGCTGCAGTGGCCGGTGCCTACTCTCTCGGTAAAAGTGCCGTGATGTC
TTCTCCTCCCCCTC (SEQ ID NO:145)

Translation:

10 LNQSDCLPRDTFCALPQLGLLCCSGRCLLFCV (SEQ ID NO:146)

Toxin Sequence:

15 Asp-Cys-Leu-Xaa3-Arg-Asp-Thr-Phe-Cys-Ala-Leu-Xaa3-Gln-Leu-Gly-Leu-Leu-Cys-Cys-Ser-
Gly-Arg-Cys-Leu-Leu-Phe-Cys-Val-^ (SEQ ID NO:147)

20 **Name:** A6.5
Species: aurisiacus
Isolated: No
Cloned: Yes

DNA Sequence:

25 ATGAAACTGACGTGCGTGATGACCGTTGCTGTGCTGTTGACCGCCTGGACATTG
GTCACGGCTGATGACTCCAGAAATGGACTGAAGAATCTTTTCCGAAGGCACGTCA
TGAAATGAAGAACCCCCGAAGCCTCTAAATTGAACAAGAGAGATGGGTGCTCTAATG
CTGGTGCAATTGTGGCATCCATCCAGGACTCTGCTGCAGCGAGATTGCATTGTT
30 GGTGCACATGAGTCGTATTCTGCTGGTACATTGTGGCTCAACGGAGGAAGTCTGC
TGCAGCAACCTTGCTTATTTCTGTGCTAACATATTGATGTCTTCACTCC
CATC (SEQ ID NO:148)

Translation:

35 MKLTCVMTVAVLFLTAWTFVTADDSRNGLKNLFPKARHEMKNPEASKLNKRDGCSNA
GAFCGIHPGLCCSEICIVWCT (SEQ ID NO:149)

Toxin Sequence:

40 Asp-Gly-Cys-Ser-Asn-Ala-Gly-Ala-Phe-Cys-Gly-Ile-His-Xaa3-Gly-Leu-Cys-Cys-Ser-Xaa1-Ile-
Cys-Ile-Val-Xaa4-Cys-Thr-^ (SEQ ID NO:150)

45 **Name:** δ-PVIA
Species: purpurascens
Isolated: Yes

Cloned: Yes

DNA Sequence:

5 ATGAAACTGACGTGCGTGATGATCGTTGCTGTGCTGTTGACTGCCTGGACATTC
 GTCACGGCTGATGACTCCAAAATGGACTGGAGAATCATTGGAAAGGCACGTGA
 CGAAATGAAGAACCGCGAAGCCTCTAAATTGGACAAAAGGAAGCCTGCTATGCGC
 CTGGTACTTTGTTGGCATAAAGCCGGCTATGCTGCAGTGAGTTGTCTCCCGG
 GCGTCTGCTTCGGTGGTTAACTGCCGTGATGTCTCTACTCCCCTGTGCTACCTGG
 10 CTTGATCTTGATCGGCGTGTGCCCTCACTGGTTATGAACCCACTGATCTTACCTCT
 CTTGAAGGACCTCTGGGGTCCAGCATCCAAATAAGCGACATCCCAATGAAAAAAA
 AAAAAA (SEQ ID NO:151)

Translation:

15 MKLTCVMIVAVLFLTAWTFVTADD SKNGLENHFWKARDEMKNREASKLDKKEACYA
 PGTFCGIKPGLCCSEFCLPGVCFGG (SEQ ID NO:152)

Toxin Sequence:

20 Xaa1-Ala-Cys-Xaa5-Ala-Xaa3-Gly-Thr-Phe-Cys-Gly-Ile-Lys-Xaa3-Gly-Leu-Cys-Cys-Ser-
 Xaa1-Phe-Cys-Leu-Xaa3-Gly-Val-Cys-Phe-Gly-# (SEQ ID NO:153)

25 **Name:** δ -PVIA-OH
Species: purpurascens
Isolated: Yes

Toxin Sequence:

30 Xaa1-Ala-Cys-Xaa5-Ala-Xaa3-Gly-Thr-Phe-Cys-Gly-Ile-Lys-Xaa3-Gly-Leu-Cys-Cys-Ser-
 Xaa1-Phe-Cys-Leu-Xaa3-Gly-Val-Cys-Phe-Gly-^ (SEQ ID NO:153)

35 **Name:** δ -PVIA[F9A]
Species: purpurascens

Toxin Sequence:

40 Xaa1-Ala-Cys-Xaa5-Ala-Xaa3-Gly-Thr-Ala-Cys-Gly-Ile-Lys-Xaa3-Gly-Leu-Cys-Cys-Ser-
 Xaa1-Phe-Cys-Leu-Xaa3-Gly-Val-Cys-Phe-Gly-^ (SEQ ID NO:154)

45 **Name:** δ -PVIA[I12A]
Species: purpurascens
Isolated:

Toxin Sequence:

Xaa1-Ala-Cys-Xaa5-Ala-Xaa3-Gly-Thr-Phe-Cys-Gly-Ala-Lys-Xaa3-Gly-Leu-Cys-Cys-Ser-Xaa1-Phe-Cys-Leu-Xaa3-Gly-Val-Cys-Phe-Gly-^ (SEQ ID NO:155)

5

Name: δ-PVIA[T8A]
Species: purpurascens

Toxin Sequence:

Xaa1-Ala-Cys-Xaa5-Ala-Xaa3-Gly-Ala-Phe-Cys-Gly-Ile-Lys-Xaa3-Gly-Leu-Cys-Cys-Ser-Xaa1-Phe-Cys-Leu-Xaa3-Gly-Val-Cys-Phe-Gly-^ (SEQ ID NO:156)

15

Name: M6.3
Species: magus
Isolated: No
Cloned: Yes

20

DNA Sequence:

ATGAAACTGACGTGCGTGATGATCGTTGCTGTGCTGTTCTTGACCACTGGACATTG
 GTCACGGCTGATGACTCCAGATATGGATTGAAGAAATCTTTTCCGAAGGCACGTCAT
 GAAATGAAGAACCTCTGAAGCCTCTAAATTGAACAAAGAGAGATGGGTGCTATAATGC
 TGGTACATTTGTGGCATCCGTCCAGGACTCTGCTGCAGCGAGTTTGCTTTATGG
 TGCATAACATTGTTGATTCTGGCTAACAGTGTGCGTTGGTTAGTGTCTTCCTCCC
 CTC (SEQ ID NO:157)

Translation:

MKLTCVMIVAVLFLTTWTFVTADDsRYGLKNLFPKARHEMKNPEASKLNKRDGNCYNA
 GTFCGIRPGLCCSEFCFLWCITFVDSG (SEQ ID NO:158)

Toxin Sequence:

Asp-Gly-Cys-Xaa5-Asn-Ala-Gly-Thr-Phe-Cys-Gly-Ile-Arg-Xaa3-Gly-Leu-Cys-Cys-Ser-Xaa1-Phe-Cys-Phe-Leu-Xaa4-Cys-Ile-Thr-Phe-Val-Asp-Ser-# (SEQ ID NO:159)

10

Name: M6.6
Species: magus
Isolated: No
Cloned: Yes

15

DNA Sequence:

ATGAAACTGACGTGCGTGATGATCGTTGCTGTGCTGTTCTGACCGACCTGGACATT
 GTCACGGCTGATGACTCCAGATATGGATTGAAGAATCTTTCCGAAGGCACGTCAT
 GAAATGAAGAACCCCTGAAGCCTCTAAATTGAACAAAGAGAGATGAATGCTATCCTCC
 TGGTACATTTGTGGCATCAAACCAGGACTTGCTGCAGCGCGATATGCTATCGTT
 5 TGTCTGCATATCATTGATTGATGTCTCCTCCCTC (SEQ ID NO:160)

Translation:

MKLTCVMIVAVLFLTTWTFVTADDsRYGLKNLFPKARHEMKNPEASKLNKRDECYPP
 10 GTFCGIKPGLCCSAICLSFVCISFDF (SEQ ID NO:161)

Toxin Sequence:

Asp-Xaa1-Cys-Xaa5-Xaa3-Xaa3-Gly-Thr-Phe-Cys-Gly-Ile-Lys-Xaa3-Gly-Leu-Cys-Cys-Ser-
 15 Ala-Ile-Cys-Leu-Ser-Phe-Val-Cys-Ile-Ser-Phe-Asp-Phe-^ (SEQ ID NO:162)

Name: M6.7
Species: magus
 20 **Isolated:** No
Cloned: Yes

DNA Sequence:

ATGAAACTGACGTGCGTGATGATCGTTGCTGTACTGTTCTGACCGCCTGGACATT
 GTCACGGCTGATGACTCCAGATATGGACTGAAGGATCTGTTCCGAAGGAACGTCA
 TGAAATGAAGAACCCCGAAGCCTCTAAATTGAACCAGAGAGAAGCCTGCTATAATG
 CTGGTTCATTTGTGGCATCCATCCAGGACTCTGCTGCAGCGAGTTTGATGTCTCCTCC
 30 GTGCATAACATTGTTGATTCTGGCTAACTGTGTGCCTGGTTGATGTCTCCTCC
 CATC (SEQ ID NO:163)

Translation:

MKLTCVMIVAVLFLTAWTFVTADDsRYGLKDLFPKERHEMKNPEASKLNQREACYNA
 35 GSFCGIHPGLCCSEFCILWCITFVDSG (SEQ ID NO:164)

Toxin Sequence:

Xaa1-Ala-Cys-Xaa5-Asn-Ala-Gly-Ser-Phe-Cys-Gly-Ile-His-Xaa3-Gly-Leu-Cys-Cys-Ser-Xaa1-
 10 Phe-Cys-Ile-Leu-Xaa4-Cys-Ile-Thr-Phe-Val-Asp-Ser-# (SEQ ID NO:165)

Name: M6.8
Species: magus
 15 **Isolated:** No
Cloned: Yes

DNA Sequence:

ATGAAACTGACGTGCATGATGATCGTTGCTGTACTGTTCTTGACCGCCTGGACATT
 5 GTCACGGCTGATGACTCCAGATATGGACTGAAGGATCTGTTCCGAAGGAACGTCA
 TGAAATGAAGAACCCCGAAGCCTCTAAATTGAACCAGAGAGAAGCCTGCTATAATG
 CTGGTACATTTGTGGCATCAAACCAGGACTTGCTGCAGCGCGATATGCTTATCGT
 TTGTCATGCATATTGATTGATGTCTTCTCCTCCCCCTC (SEQ ID NO:166)

Translation:

10 MKLTCMMIVAVLFLTAWTFVTADD SRYGLKDLFPKERHEMKNPEASKLNQREACYNA
 GTFCGIKPGLCCSAICLSFVCISFDF (SEQ ID NO:167)

Toxin Sequence:

15 Xaa1-Ala-Cys-Xaa5-Asn-Ala-Gly-Thr-Phe-Cys-Gly-Ile-Lys-Xaa3-Gly-Leu-Cys-Cys-Ser-Ala-
 Ile-Cys-Leu-Ser-Phe-Val-Cys-Ile-Ser-Phe-Asp-Phe- (SEQ ID NO:168)

20 **Name:** E6.4
Species: ermineus
Isolated: No
Cloned: Yes

DNA Sequence:

ATGAAACTGACGTGCCTGATGATCGTTGCTGTGCTGTTCTTGACTGCCTGGACATT
 GTCACGGCTGATGACTCCAAAAATGGACTGGAGAATCATTGGAAAGGCACGTGA
 CGAAATGAAGAACCGCGAAGCCTCTAAATTGGACAAAAAGGAAGCCTGCTATCCGC
 30 CTGGTACTTTGTGGCATAAAGCCGGCTATGCTGCAGTGAGTTGTGTTACCGG
 CCGTCTGCGTCGGTGGTTAAGTGCCTGATGTCTTCTCCTCCCCCTC (SEQ ID NO:169)

Translation:

35 MKLTCVMIVAVLFLTAWTFVTADD SKNGLENHFWKARDEMKNREASKLDKKEACYP
 PGTFCGIKPGLCCSELCLPAVCVGG (SEQ ID NO:170)

Toxin Sequence:

40 Xaa1-Ala-Cys-Xaa5-Xaa3-Xaa3-Gly-Thr-Phe-Cys-Gly-Ile-Lys-Xaa3-Gly-Leu-Cys-Cys-Ser-
 Xaa1-Leu-Cys-Leu-Xaa3-Ala-Val-Cys-Val-Gly-# (SEQ ID NO:171)

45 **Name:** P6.4
Species: purpurascens
Isolated: No
Cloned: Yes

DNA Sequence:

5 ATGAAACTGACGTGCATGATCGTTGCTGTGCTGTTCTGACTGCCTGGACATT
 GTCACGGCTGATGACTCCAAAAATGGACTGGAGAATCATTGGAAAGGCACGTGA
 CGAAATGAAGAACCGCGAAGCCTCTAAATTGGACAAAAAGGAAGCCTGCTATCCGC
 CTGGTACTTTGTGGCATAAAGCCCAGGCTATGCTGCAGTGAGTTGTGTTACCGG
 CCGTCTCGTCGGTGGTTAACTGCCGTGATGTCTCTCCTCCCCTC (SEQ ID NO:172)

10 Translation:

MKLT CMMIVAVLFLTAWTFVTADDSKNGLENHFWKARDEMKNREASKLDKKEACYP
 PGTFCGIKPGLCCSELCLPAVCVGG (SEQ ID NO:173)

15 Toxin Sequence:

Xaa1-Ala-Cys-Xaa5-Xaa3-Xaa3-Gly-Thr-Phe-Cys-Gly-Ile-Lys-Xaa3-Gly-Leu-Cys-Cys-Ser-
 Xaa1-Leu-Cys-Leu-Xaa3-Ala-Val-Cys-Val-Gly-# (SEQ ID NO:174)

20 **Name:** δ-SVIE [D1E]
Species: striatus
Isolated: Yes
Cloned: Yes

25 DNA Sequence:

ATGAAACTGACGTGCATGATCGTTGCTGTGCTGTTCTGACCACTGGACATT
 GTCACGGCTGATGACTCCAGATATGGATTGAAGAATCTTTCCGAAGGCACGTCA
 30 GAAATGAAGAACCCCGAAGCCTCTAAATTGAACAAGAGAGAAGGGTGCTCTAGTG
 GTGGTACATTTGTGGCATCCATCCAGGACTCTGCTGCAGCGAGTTGCTTCTTG
 GTGCATAAACATTATTGATTGATGTCTCTCCTCCCCTC (SEQ ID NO:175)

Translation:

35 MKLTCVMIVAVLFLTTWTFVTADDSRYGLKNLFPKARHEMKNPEASKLNKREGCSSG
 GTFCGIHPGLCCSEFCFLWCITFID (SEQ ID NO:176)

Toxin Sequence:

40 Xaa1-Gly-Cys-Ser-Ser-Gly-Gly-Thr-Phe-Cys-Gly-Ile-His-Xaa3-Gly-Leu-Cys-Cys-Ser-Xaa1-
 Phe-Cys-Phe-Leu-Xaa4-Cys-Ile-Thr-Phe-Ile-Asp-^ (SEQ ID NO:177)

45 **Name:** δ-SVIE
Species: striatus
Isolated: Yes

Cloned: Yes

DNA Sequence:

5 ATGAAACTGACGTGCGTGATGATCGTTGCTGTGCTGTTGACCACTGGACATTC
 GTCACGGCTGATGACTCCAGATATGGATTGAAGAATCTTTCCGAAGGCACGTCA
 GAAATGAAGAACCCCGAAGCCTCTAAATTGAACAAGAGAGATGGGTGCTCTAGTGG
 TGGTACATTTGTGGCATCCATCCAGGACTCTGCTGCAGCGAGTTGCTTCTTGG
 TGCATAAACATTTATTGATTGATGTCTCTCCTCCCCTC (SEQ ID NO:178)

10 **Translation:**

MKLCVMIVAVLFLTTWTFVTADDsRYGLKNLFPKARHEMKNPEASKLNKRDGCSSG
 GTFCGIHPGLCCSEFCFLWCITFID (SEQ ID NO:179)

15 **Toxin Sequence:**

Asp-Gly-Cys-Ser-Ser-Gly-Gly-Thr-Phe-Cys-Gly-Ile-His-Xaa3-Gly-Leu-Cys-Cys-Ser-Xaa1-
 Phe-Cys-Phe-Leu-Xaa4-Cys-Ile-Thr-Phe-Ile-Asp-^ (SEQ ID NO:180)

20 **Name:** δ-NgVIA
Species: striolatus
Isolated: Yes

25 **Toxin Sequence:**

Ser-Lys-Cys-Phe-Ser-Xaa3-Gly-Thr-Phe-Cys-Gly-Ile-Lys-Xaa3-Gly-Leu-Cys-Cys-Ser-Val-
 Arg-Cys-Phe-Ser-Leu-Phe-Cys-Ile-Ser-Phe-Xaa1-^ (SEQ ID NO:181)

30 **Name:** C6.2
Species: catus
Isolated: No
 35 **Cloned:** Yes

DNA Sequence:

40 ATGAAACTGACGTGATGATCGTTGCTGTGCTGTTGACCACTGGACATTC
 GTCACGGCTGATGACTCCAGAAATGGACTGAAGAATCTTTCCGAAGGCACGTCA
 TGAAATGAAGAACCCCGAAGCCTCTAAATTGAACAAGAGAGATGGGTGCTCTAATG
 CTGGTGCATTTGTGGCATCCATCCAGGACTCTGCTGCAGCGAGCTTGCTGGTT
 GGTGCACATGAGTGCTATTCTCTGGTACATTGTGGCTTCAACGGAGGACTCTGC
 TGCAGCAACCTTGCTTATTCGTGTGCTAACATTCTCGTGTGCTTCTATTCC
 45 CCTC (SEQ ID NO:182)

Translation:

MKLT CMMIVAVLFLTAWTFVTADD SRNGLKNLFPKARHEMKNPEASKLNKRYGCSNA
 GAFCGIHPGLCCSELCLVWCT (SEQ ID NO:183)

5 **Toxin Sequence:**

Xaa5-Gly-Cys-Ser-Asn-Ala-Gly-Ala-Phe-Cys-Gly-Ile-His-Xaa3-Gly-Leu-Cys-Cys-Ser-Xaa1-
 Leu-Cys-Leu-Val-Xaa4-Cys-Thr-^ (SEQ ID NO:184)

10 **Name:** C6.3
Species: catus
Isolated: No
Cloned: Yes

15 **DNA Sequence:**

ATGAAACTGACGTGTATGATGATCGTTGCTGTGCTGTTCTTGACCGCCTGGACATT
 GTCACGGCTGATGACTCCAGATATGGACTGAAGAATCTTTCCGAAGGCACGTCAT
 20 GAAATGAAGAACCCCGAAGCCTCTAAATTGAACAAGAGATATGGGTGCTCTAATGC
 TGGTGCATTTGTGGCATCCATCCAGGACTCTGCTGCAGCGAGCTTGCCTGGGTTG
 GTGCACATGAGTGCTATTCTACTGGTACATTTGTGGCTAACACCGGAGGACTCTGCT
 GCAGCAACCTTGCTTATTCGTGTGCTAACATT CGTATGTCTCTATTCCC
 CTC (SEQ ID NO:185)

25 **Translation:**

MKLT CMMIVAVLFLTAWTFVTADD SRYGLKNLFPKARHEMKNPEASKLNKRYGCSNA
 GAFCGIHPGLCCSELCLGWCT (SEQ ID NO:186)

30 **Toxin Sequence:**

Xaa5-Gly-Cys-Ser-Asn-Ala-Gly-Ala-Phe-Cys-Gly-Ile-His-Xaa3-Gly-Leu-Cys-Cys-Ser-Xaa1-
 Leu-Cys-Leu-Gly-Xaa4-Cys-Thr-^ (SEQ ID NO:187)

35 **Name:** Di6.3
Species: distans
Isolated: No
Cloned: Yes

DNA Sequence:

ATGAAACTGACGTGTCTGATGATCGTTGCTGTGCTGTTCTTGACCGCCTGGACATT
 40 GTCACGGCTGATGACTCCAGAAATGGATTGGAGAATCTCTCCGAAGGCACCTCA
 CGAAATGAAGAACCCCGAAGCCTCTAAATCGAACAGAGATATGAGTGCTATCTAC
 TGGTACATTTGTGGCATCACCGGAGGACTCTGCTGCAGAACCTTGCTTATTTT

CGTGTGCTAACATTTCGTATGTCTCCTCCCATC (SEQ ID NO:188)

Translation:

5 MKLTCLMIVAVLFLTAWTFVTADDSRNGLENLSPKAPHEMKNPEASKSNKRYECYLLV
HFCGINGGLCCSNLCLFFVCLTFS (SEQ ID NO:189)

Toxin Sequence:

10 Xaa5-Xaa1-Cys-Xaa5-Leu-Leu-Val-His-Phe-Cys-Gly-Ile-Asn-Gly-Gly-Leu-Cys-Cys-Ser-Asn-
Leu-Cys-Leu-Phe-Phe-Val-Cys-Leu-Thr-Phe-Ser-^ (SEQ ID NO:190)

15 **Name:** Rg6.1
Species: regius
Isolated: No
Cloned: Yes

DNA Sequence:

20 TTGAGCAAGAGAGACTGCCTCCTGACTACACGATTGTGCCTCAATATGGGTCTG
TGCTGCAGCGACAAGTCATGCTCGTGCCTGCCGTATGTCTTCTCCTCCCTC
(SEQ ID NO:191)

25 **Translation:**

LSKRDCLPDYTICAFNMGLCCSDKMLVCLP (SEQ ID NO:192)

Toxin Sequence:

30 Asp-Cys-Leu-Xaa3-Asp-Xaa5-Thr-Ile-Cys-Ala-Phe-Asn-Met-Gly-Leu-Cys-Cys-Ser-Asp-Lys-
Cys-Met-Leu-Val-Cys-Leu-Xaa3-^ (SEQ ID NO:193)

35 **Name:** Rg6.3
Species: regius
Isolated: No
Cloned: Yes

40 **DNA Sequence:**

TTGAACAAGAGAACATCTGCTTCCTGACTACATGTTTGTGGCGTCAATGTGTTTC
TGTGCTGCAGTGGCAACTGCCTCTCATCTGCGTGCCTGATGTCTTACTCCCTC
(SEQ ID NO:194)

45 **Translation:**

LNKRIICFPDYMFCGVNVFLCCSGNCLLICVP (SEQ ID NO:195)

Toxin Sequence:

5 Ile-Ile-Cys-Phe-Xaa3-Asp-Xaa5-Met-Phe-Cys-Gly-Val-Asn-Val-Phe-Leu-Cys-Cys-Ser-Gly-
Asn-Cys-Leu-Leu-Ile-Cys-Val-Xaa3-^ (SEQ ID NO:196)

10 **Name:** Gm6.2
Species: gloriamaris
Isolated: No
Cloned: Yes

DNA Sequence:

15 ATGAAACTGACGTGCATGATGATCGTTGCTGTGCTGTTCTTGACCGCCTGGACATTG
GTCACGGCTGTGCCTCACTCCAGCAATGCGTTGGAGAATCTTATCTGAAGGCACAT
CATGAAATGAACAACCCCGAAGACTCTGAATTGAACAAGAGGTGCTATGATGGTGG
GACAGGTTGTGACTCTGGAAACCAATGCTGCAGTGGCTGGTGCATTTCGCCTGCCT
20 CTAAAACGTGCGTATGTCTTCCTCCCCCTC (SEQ ID NO:197)

Translation:

25 MKLTCMMIVAVLFLTAWTFVTAVPHSSNALENLYLKAHHEMNNPEDSELNKRCYDGG
TGCDSGNQCCSGWCIFACL (SEQ ID NO:198)

Toxin Sequence:

30 Cys-Xaa5-Asp-Gly-Gly-Thr-Gly-Cys-Asp-Ser-Gly-Asn-Gln-Cys-Cys-Ser-Gly-Xaa4-Cys-Ile-
Phe-Ala-Cys-Leu-^ (SEQ ID NO:199)

35 **Name:** Da6.1
Species: dalli
Isolated: No
Cloned: Yes

DNA Sequence:

40 ATGAAACTGACGTGCATTATGATCGTTGCTGTGCTGTTCTTGACCGCCTGGACATTG
GTCACGGCTGTGCCTCACTCCAGCAATGCGTTGGAGAATCTTATCTGAAGGCACAT
CATGAAATGAACAACCCCGAGGGACTCTGAATTGAACAAGAGGTGCTATGATGGTGG
GACAGGTTGTGACTCTGGAAACCAATGCTGCAGTGGCTGGTGCATTTCGTCTGCCT
CTAAAACGTGCCGTATGTCTCTCCCCATC (SEQ ID NO:200)

45 **Translation:**

MKLTCIMIVAVLFLTAWTFVTAVPHSSNALENLYLKAHHEMNNPEDSELNKRCYDGGT
GCDSGNQCCSGWCIFVCL (SEQ ID NO:201)

Toxin Sequence:

5 Cys-Xaa5-Asp-Gly-Gly-Thr-Gly-Cys-Asp-Ser-Gly-Asn-Gln-Cys-Cys-Ser-Gly-Xaa4-Cys-Ile-
Phe-Val-Cys-Leu-^ (SEQ ID NO:202)

10 **Name:** Pn6.6
Species: pennaceus
Isolated: No
Cloned: Yes

15 **DNA Sequence:**

ATGAAACTGACGTGCGTGATGATCGTTGCTGTGCTGTTCTGACCGCCTGGACAGTC
 GTCACGGCTGTGCCTCACTCCAACAAGCGGTTGGCGAATCTTATCTGAAGGCACGT
 CACGAAATGAAAAACCCGAAGCCTCTAATGTGGACAAGAGGTGCTTGAGAGTTG
 20 GGTAGCTTGTGAGTCTCCAAAACGATGCTGCAGTCACGTGTGCCTTTCGTCTGCAC
 CTGAAACTGCCGTGATGTCTTCTCCTCCCCCTC (SEQ ID NO:203)

Translation:

25 MKLTCVMIVAVLFLTAWTVVTAVPHSNKRLANLYLKARHEMKNPEASNVDKRCFESW
VACESPKRCCSHVCLFVCT (SEQ ID NO:204)

Toxin Sequence:

30 Cys-Phe-Xaa1-Ser-Xaa4-Val-Ala-Cys-Xaa1-Ser-Xaa3-Lys-Arg-Cys-Cys-Ser-His-Val-Cys-Leu-
Phe-Val-Cys-Thr-^ (SEQ ID NO:205)

35 **Name:** Di6.5
Species: distans
Isolated: No
Cloned: Yes

DNA Sequence:

40 ATGAAACTGACGTGTATGTTGATCATCGCTGTGCTGTTCTGACGGCCTGTCAACTC
 TCTACAAATGCGAGTTACGCCAGAAGTAAGCAGAAGCATCGTGTCTGAGGTCGAC
 TGACAAAAACTCCAAGTTGACCCAGCGTTGCAATGAAGCTCAAGAACATTGCACTC
 AAAATCCTGACTGCTGCAGTGAGTCTTGAATAAGTTGTCGGCAGATGCTGTCAG
 45 ACTGATCTGATGTCTTCTCCTCCCCATC (SEQ ID NO:206)

Translation:

MKLTCMLIIAVLFLTACQLSTNASYARSQKHRVLRSTDNSKLTQRCNEAQEHCTQN
PDCCSESCNKFVGRCLSD (SEQ ID NO:207)

5 **Toxin Sequence:**

Cys-Asn-Xaa1-Ala-Gln-Xaa1-His-Cys-Thr-Gln-Asn-Xaa3-Asp-Cys-Cys-Ser-Xaa1-Ser-Cys-
Asn-Lys-Phe-Val-Gly-Arg-Cys-Leu-Ser-Asp-^ (SEQ ID NO:208)

10 **Name:** Af6.10
Species: ammiralis
Isolated: No
Cloned: Yes

15 **DNA Sequence:**

ATGAAACTGACGTGCCTGATGATCGTTGCTGTGCTGTTCTTGACCGCCTGGACATTG
GTCACGGCTGTGCCTGACTCCAGCAATGCGTTGGAGAATCTTATCTGAAGGCACAT
20 CATGAAATGAACAACCCCGAAGACTCTGAATTGAACAAGAGGGTCTATGATGGTGG
GACAAGTTGTAACACTGGAAACCAATGCTGCAGTGGCTGGTCATTTCCCTGCCT
CTAAAACGCCGTGATGTCTTCTCTCCCCTC (SEQ ID NO:209)

5 **Translation:**

25 MKLTCLMIVAVLFLTAWTFVTAVPDSSNALENLYLKAHHEMNNPEDSELNKRCYDGG
TSCNTGNQCCSGWCIFLCL (SEQ ID NO:210)

30 **Toxin Sequence:**

Cys-Xaa5-Asp-Gly-Gly-Thr-Ser-Cys-Asn-Thr-Gly-Asn-Gln-Cys-Cys-Ser-Gly-Xaa4-Cys-Ile-
Phe-Leu-Cys-Leu-^ (SEQ ID NO:211)

35 **Name:** Tx6.10
Species: textile
Isolated: No
Cloned: Yes

40 **DNA Sequence:**

GGCATTACCTAAAACATCACCAAGATGAAACTGACGTGCATGATGATCGTTGCTGT
GCTGTTCTTGACCGCCTGGACATTCTGCACGGCTGCGCCTCACTCCAGCAATGCGTT
GGAGAAATCTTATCTGAAGGCACATCATGAAATGAACAACCCGAAGCCTCTGAAT
45 TGAACAAAGAGGGTCTATGATAGTGGGACAAGTTGTAACACTGGAAACCAATGCTGC
AGTGGCTGGTGCATTTCTGCCTCTAAACTACCGTGATGTCTCTCCTCCC
CTC (SEQ ID NO:212)

Translation:

5 MKLTCMMIVAVLFLTAWTFVTAAPHSSNALENLYLKAHHEMNNPEASELNKRCYDSG
TSCNTGNQCCSGWCIFVSCL (SEQ ID NO:213)

Toxin Sequence:

10 Cys-Xaa5-Asp-Ser-Gly-Thr-Ser-Cys-Asn-Thr-Gly-Asn-Gln-Cys-Cys-Ser-Gly-Xaa4-Cys-Ile-
Phe-Val-Ser-Cys-Leu-^ (SEQ ID NO:214)

15 **Name:** Gm6.4
Species: gloriamaris
Isolated: No
Cloned: Yes

DNA Sequence:

20 ATGAAACTGACGTGCATGATGATCGTTGCTGTGCTGTTCTGACAGCCTGGACGCTA
GTCATGGCTGATGACTCCAACAATGGACTGGCGAATCTTTTCGAAATCACGTGAC
GAAATGGAGGACCCCGAAGCTCTAAATTGGAGAAAAGGGATTGCCAAGCACTATG
GGATTATTGTCCAGTACCGCTCTGTCATGGGTGATTGCTGCTATGGCTTAATCTGT
GGCCCTTCGTCTGCATTGGATGGATGTCTTACTCCCATC (SEQ ID NO:215)

Translation:

MKLTCMMIVAVLFLTAWTLVMADDNNGLANLFSKRDEMEDPEASKLEKRDCQAL
WDYCPVPLLSSGDCCYGLICGPVCIGW (SEQ ID NO:216)

30 **Toxin Sequence:**

Asp-Cys-Gln-Ala-Leu-Xaa4-Asp-Xaa5-Cys-Xaa3-Val-Xaa3-Leu-Leu-Ser-Ser-Gly-Asp-Cys-
Cys-Xaa5-Gly-Leu-Ile-Cys-Gly-Xaa3-Phe-Val-Cys-Ile-Gly-Xaa4-^ (SEQ ID NO:217)

35 **Name:** Om6.2
Species: omaria
Isolated: No
Cloned: Yes

DNA Sequence:

40 ATGAAACTGACGTGCCTGATGATCGTTGCTGTGCTGTTCTGACCGCCTGGACATTG
GTCATGGCTGATGACTCCAACATGGACTGGCAAATCTTTCTCGAAATCACGTGAC
GAAATGGAGGATACCGATCCTCTAAATTGGAGAACAGAAAAACTGCCAAAGAAG
GTGGGATTGGTCCAGGATCGCTCGTTGGAGTGATAACTGCTGCGGTGGCTTAAT

CTGTTTCTGTTCTGCGTTGATAGTGTGCTCTCCTCCCT (SEQ ID NO:218)

Translation:

5 MKLTCLMIVAVLFLTAWTFVMADDNNGLANLFSKRDEMEDDPSKLENRKTCQRR
WDFCPGSLVGVITCCGGICFLFFCV (SEQ ID NO:219)

Toxin Sequence:

10 Lys-Thr-Cys-Gln-Arg-Arg-Xaa4-Asp-Phe-Cys-Xaa3-Gly-Ser-Leu-Val-Gly-Val-Ile-Thr-Cys-
Cys-Gly-Gly-Leu-Ile-Cys-Phe-Leu-Phe-Phe-Cys-Val-^ (SEQ ID NO:220)

15 **Name:** Da6.3
Species: dalli
Isolated: No
Cloned: Yes

20 **DNA Sequence:**

25 ATGAAACTGACGTGTGATGATCGTTGCTGTGCTGTTCTGACAGCCTGGACGCTA
GTCATGGCTGATGACTCCAACAATGGACTGGCGAATCTTTTCGAAATTACGTGAC
GAAATGGAGGACCCCGAAGGTTCTAAATTGGAGAAAAGGATTGCCAAGAAAAAT
GGGATTATTGTCCAGTACCGTTCTGGGATCGAGGTATTGCTGCGATGGCTTATCT
GTCCATTTCTTCTGCGCTTGATAGTGTCTATTCCCCTC (SEQ ID NO:221)

Translation:

30 MKLTCVMIVAVLFLTAWTLVMADDNNGLANLFSKLRDEMEDPEGSKLEKKDCQEKG
WDYCPVPFLGSRYCCDGFIICPSFFCA (SEQ ID NO:222)

Toxin Sequence:

35 Asp-Cys-Gln-Xaa1-Lys-Xaa4-Asp-Xaa5-Cys-Xaa3-Val-Xaa3-Phe-Leu-Gly-Ser-Arg-Xaa5-Cys-
Cys-Asp-Gly-Phe-Ile-Cys-Xaa3-Ser-Phe-Phe-Cys-Ala-^ (SEQ ID NO:223)

40 **Name:** Da6.7
Species: dalli
Isolated: No
Cloned: Yes

45 **DNA Sequence:**

ATGAAACTGACGTGCGTGATGATCGTTGCTGTGTTCTGACAGCCTGGACGCTA

5 GTCATGGCTGATGACTCCAACAATGGACTGGCGAATCATTGGAAATCACGTGAC
 GAAATGGAGGACCCTGAAGCTCTAAATTGGAGAAAAGGGATTGCCAAGGCGAATG
 GGAGTTTGTATAGTACCGTCCTGGATTGTATTGCTGCCCTGGCTTATCTGT
 GGCCCTTCGTCTCGTTGATATCTGATGTCTTATCCCCTC (SEQ ID NO:224)

10 **Translation:**

15 MKLTCVMIVAVLFLTAWTLVMADDSNNGLANHFWKSREDEMPEASKLEKRDCQGE
 WEFCIVPVLGFVYCCPWLICGPFVCVDI (SEQ ID NO:225)

20 **Toxin Sequence:**

25 Asp-Cys-Gln-Gly-Xaa1-Xaa4-Xaa1-Phe-Cys-Ile-Val-Xaa3-Val-Leu-Gly-Phe-Val-Xaa5-Cys-
 Cys-Xaa3-Xaa4-Leu-Ile-Cys-Gly-Xaa3-Phe-Val-Cys-Val-Asp-Ile-^ (SEQ ID NO:226)

30 **Name:** Pn6.5
Species: pennaceus
Isolated: No
 35 **Cloned:** Yes

40 **DNA Sequence:**

45 ATGAAACTGACGTGCCTGATGATCATTGCTGTGCTGTTCTGACCGCCTGGACATTG
 50 GTCATGGCTGATGACCCAGAGATGAACCGGAGGCACGTGACGAAATGAACCCCGC
 AGCCTCTAAATTGAACGAGAGAGGGCTGCCTGAAGTTGATTATTTTGCAGCATACC
 55 GTTTGTGAACAAACGGGCTATGCTGCAGTGGCAATTGTGTTTGTCTGCACACCCCA
 AGGGAAGTAAAAGTGTGATGTCTTCTCTTCCATC (SEQ ID NO:227)

60 **Translation:**

65 MKLTCLMIIAVLFLTAWTFVMADDPRDEPEARDEMNPAAASKLNERGCLEVDYFCGIPF
 VNNGLCCSGNCVFVTPQGK (SEQ ID NO:228)

70 **Toxin Sequence:**

75 Gly-Cys-Leu-Xaa1-Val-Asp-Xaa5-Phe-Cys-Gly-Ile-Xaa3-Phe-Val-Asn-Asn-Gly-Leu-Cys-Cys-
 Ser-Gly-Asn-Cys-Val-Phe-Val-Cys-Thr-Xaa3-Gln-# (SEQ ID NO:229)

80 **Name:** Marm6
Species: marmoreus
Isolated: No
 85 **Cloned:** Yes

90 **DNA Sequence:**

GGTCGACATCATCATCATCGATCCATCTGTCCATCCATCTGTCCATCCATCCATT
 5 TCATTCACTGCCAAACTGTCATAAAATATTGAGTCTCTCTTCTGTTTATCTGACA
 GATTGAACGAGAGAGACTGCCTTAATGTTGATTATTTTGCGGCATACCGTTGTGA
 ACAACGGGCTATGCTGCAGTGGCAATTGTGTTTGTCTGCACACCCCAAGGGAAGT
 10 AAAACTGCCGTGATGTCTCTCTCCCTCTAGTAGTAGTAGTAGGGCGGCCCTAGAG
 GATCCAAGCTTACGTACGCGTGCATGCGACGTACAGCTCTATAGTGTACACCTA
 AATTCAATTCACTGGCCGTCCGTTTACAACGTCGTGACTGGGAAAACCTGGCGTT
 ACCCAACTTAATCGCCTGCAGCACAT (SEQ ID NO:230)

10 **Translation:**

NERDCLNVDYFCGIPFVNNGLCCSGNCVFVCTPQGK (SEQ ID NO:231)

15 **Toxin Sequence:**

Cys-Leu-Asn-Val-Asp-Xaa5-Phe-Cys-Gly-Ile-Xaa3-Phe-Val-Asn-Asn-Gly-Leu-Cys-Cys-Ser-
 Gly-Asn-Cys-Val-Phe-Val-Cys-Thr-Xaa3-Gln-# (SEQ ID NO:232)

20 **Name:** Marm15
Species: marmoreus
Isolated: No
Cloned: Yes

25 **DNA Sequence:**

TCGACATCATCATCATCGATCCATCTGTCCATCCATTCAATTGCTGCCAA
 ACTGTCTATAAAATATTGAGTCTCTCTTCTGTTTATCTGACAGATTGGACAAGAGA
 GAGTGCGCTGGAAGCTGATTATTATTGCGTCTTACCGTTGTGGCAACGGGATGTGC
 30 TGCAGTGGCATTGTGTTTGTCTGCATAGCCC (SEQ ID NO:233)

35 **Translation:**

LDKRECLEARYYCVLPFVGNGMCCSGICVFV р IAQRFKTV (SEQ ID NO:234)

35 **Toxin Sequence:**

Xaa1-Cys-Leu-Xaa1-Ala-Asp-Xaa5-Xaa5-Cys-Val-Leu-Xaa3-Phe-Val-Gly-Asn-Gly-Met-Cys-
 Cys-Ser-Gly-Ile-Cys-Val-Phe-Val-Cys-Ile-Ala-Gln-Arg-Phe-Lys-Thr-Val-^ (SEQ ID NO:235)

40 **Name:** Marm10
Species: marmoreus
Isolated: No
 45 **Cloned:** Yes

DNA Sequence:

GTACCGGTCCGGAATTCCCGGGTCGACATCATCATCATCGATCCATCTGTCCATCCA
 TCCATCCATTCAATTCAATTGCTGCCAAACTGTCAAAACATTGAGTCTCTCTTCTG
 5 TTTTATCTGACAGATTGAACGAGAGAGACTGCCTGAACCTGATTATGTTGCCGC
 ATACC GTTGTGTTCAACGGGCTATGCTGCAGTGGAAATTGTGTTTATCTGCATAG
 CCCAAAAGTATTAAAACGCCGTGATGTCTTCTATTCCCATCTAGTAGTAGTAGGC
 10 CCGCTCTAGAGGATCCAAGCTTACGTACCGTGCATGCAGTCATAGCTCTTCTAT
 AGTGTCACTAAATTCAATTCAACTGGCCGTCGTTACAACGTCGTGACTGGGAAA
 CCCTGGCGTTACCCAACCTTAATGCCCTGCAGCACATCCCCCTTCGCCAGCTGGCG
 TAATAGCCGAAGAGGCCGCACCGATGCCCTCCAACAGTTGCGCAGCCTGAAT
 GGCGAATGGGG (SEQ ID NO:236)

Translation:

15 LNERDCLEPDYVCGIPFVFNLCCSGICVFICIAQKY (SEQ ID NO:237)

Toxin Sequence:

Asp-Cys-Leu-Xaa1-Xaa3-Asp-Xaa5-Val-Cys-Gly-Ile-Xaa3-Phe-Val-Phe-Asn-Gly-Leu-Cys-
 20 Cys-Ser-Gly-Ile-Cys-Val-Phe-Ile-Cys-Ile-Ala-Gln-Lys-Xaa5-^ (SEQ ID NO:238)

25 **Name:** Marm14
Species: marmoreus
Isolated: No
Cloned: Yes

DNA Sequence:

30 GGTACGCCTGCAGGTACCGGTCCGGAATTCCCGGGTCGACATCATCATCATCGA
 TCCATCTGTCCATCCATCTATTCAATTGCTGTCAAACGTAAATACATATTAGAA
 TCTCTCTTCTGTTGTATCTGACAGATTGGAGAAAAGGGCGTGCAGAAAAAAATGG
 GAATATTGTATAGTACCGATCCTGGATTGCTATATTGCTGCCCTGGCTTAATCTGTG
 35 GTCCTTCGTCTGCGTTGATAGTGTATCTCTCCCATCTAGTAGTAGTAGAGCG
 GCCGCTCTAGAGGATCCAAGCTACGTACCGTGCATGCAGTCATAGCTCTCTA
 TAGTGTCACTAAATTCAATTCAACTGGCCGTCGTTACAACGTCGTGACTGGGAAA
 ACCCTGGCGTTACCCAACCTTAATGCCCTGCAGCACATCCCCCTTCGCCAGCTGGC
 GTAATAAGCGAAGAGGCCGCACCGATGCCCTCCAACAGTTGCGCAGCCTGAA
 TGGCGAAATGGGACGCGCCCTG (SEQ ID NO:239)

40

Translation:

LEKRACSKKWEYCIVPILGFVYCCPGLICGPFVCV (SEQ ID NO:240)

45 **Toxin Sequence:**

Ala-Cys-Ser-Lys-Lys-Xaa4-Xaa1-Xaa5-Cys-Ile-Val-Xaa3-Ile-Leu-Gly-Phe-Val-Xaa5-Cys-Cys-

Xaa3-Gly-Leu-Ile-Cys-Gly-Xaa3-Phe-Val-Cys-Val-[^] (SEQ ID NO:241)

5 **Name:** Omaria14
Species: omaria
Isolated: No
Cloned: Yes

10 **DNA Sequence:**

10 AAAGCCGGTACGCCTGCAGGTACCGGTCCGGAATTCCCGGGTCGACATCATCATCA
TCATCGATCCATCTGTCCATCCATCCATTCACTGCCAAACTGTCATAAAT
ATTGAGTCTCTTTCTGTTTATCTGACAGATTGAACGAGAGAGACTGCCTTAAT
GTTGATTATTTGTGGCATACCGTTGTGAACAACGGGCTATGCTGCAGTGGCAAT
15 TGTGTTTTGTCTGCACACCCCAAGGAAAGTAAAAGTCCGATGTCTCTCTCC
CCTCTAGTAGTAGTAGGCCGCGCTCTAGAGGATCCAAGCTTACGTACGGCGTGCAT
GCGACGTCATAGCTCTTCTATAGTGTACCTAAATTCAATTCAACTGGCCGTCGTTTA
CAACGTCGTGACTGGAAAACCCCTGGCGTTACCCAACCTAATGCCCTGCAGCACAT
20 CCCCTTCGCCAGCTGGCGTAATAGCGAAGAGGCCGACCGATGCCCTCCA
ACAGTTGCGCAGCCTGAATGGCGAATGGGACGCGCCCT (SEQ ID NO:242)

25 **Translation:**

25 LNERDCLNVDYFCGIPFVNNGLCCSGNCVFCLHTPREVKLP (SEQ ID NO:243)

30 **Toxin Sequence:**

30 Asp-Cys-Leu-Asn-Val-Asp-Xaa5-Phe-Cys-Gly-Ile-Xaa3-Phe-Val-Asn-Asn-Gly-Leu-Cys-Cys-
Ser-Gly-Asn-Cys-Val-Phe-Cys-Leu-His-Thr-Xaa3-Arg-Xaa1-Val-Lys-Leu-Xaa3-[^] (SEQ ID
NO:244)

35 **Name:** O6.4
Species: obscurus
Isolated: No
Cloned: Yes

40 **DNA Sequence:**

40 cgatccatctgtccatccatccattcattcattgccaactgtAACAAATTCAAGTCTCTTCTGTTGTCTGACAGATCGAAA
CGGTGCCTTGTACGGTACACCTTGTGACTGGCTGACCATTGCGGGTATGGAGTGC
TGCAGTAAAAGTGTCTTATGATGTGCTGGTAAAAGTCCGATGTCTTACTCC
CCTC (SEQ ID NO:245)

45 **Translation:**

45 RSKRCLVYGTCDWLTAGMECCSKKCFMMCW (SEQ ID NO:246)

Toxin Sequence:

5 Cys-Leu-Val-Xaa5-Gly-Thr-Xaa3-Cys-Asp-Xaa4-Leu-Thr-Ile-Ala-Gly-Met-Xaa1-Cys-Cys-Ser-
Lys-Lys-Cys-Phe-Met-Met-Cys-Xaa4-^ (SEQ ID NO:247)

10 **Name:** R6.4
Species: radiatus
Isolated: No
Cloned: Yes

DNA Sequence:

15 ATTGAACCAGAGAGACTGCCATGAAGTTGGTGAATTGTGGCTTACCGTTAATAAA
GAACGGGCTATGCTGCAGATTGTTAGGTGTGCGCAAAAGTGTAA
CTGCCGTGATGTCTTCACTCCCAT (SEQ ID NO:248)

Translation:

20 LNQRDCHEVGEFCGLPLIKNGLCCSQICLGVCAKVF (SEQ ID NO:249)

Toxin Sequence:

25 Asp-Cys-His-Xaa1-Val-Gly-Xaa1-Phe-Cys-Gly-Leu-Xaa3-Leu-Ile-Lys-Asn-Gly-Leu-Cys-Cys-
Ser-Gln-Ile-Cys-Leu-Gly-Val-Cys-Ala-Lys-Val-Phe-^ (SEQ ID NO:250)

30 **Name:** R6.6
Species: radiatus
Isolated: No
Cloned: Yes

DNA Sequence:

35 ATTAGACAAGAAAGAGTCAGTGCCTGGCAATTGTGGCATATCGGTCTTGG
AAGCTACCTATGCTGCAGTGGCCGGTGTATTGCTGCTAGTTGAAGTGGCG
TGATGTCTTCACTCCCCCT (SEQ ID NO:251)

10 Translation:

LDKKECTANGEFCGISVFGSYLCCSGRCVFVCI (SEQ ID NO:252)

Toxin Sequence:

45 Xaa1-Cys-Thr-Ala-Asn-Gly-Xaa1-Phe-Cys-Gly-Ile-Ser-Val-Phe-Gly-Ser-Xaa5-Leu-Cys-Cys-
Ser-Gly-Arg-Cys-Val-Phe-Val-Cys-Ile-^ (SEQ ID NO:253)

5 **Name:** R6.7
Species: radiatus
Isolated: No
Cloned: Yes

DNA Sequence:

10 ATTGGACAAGAAAGAGTCACCAATGGTGAATTTGTGGCATATCGGTCTTGC
AAGCTTCCTATGCTGCAGTGGCCTGTGTATTCGTCTGCATCTAGCTGAAC TGCCG
TGATGTCTTCTCTCCCC (SEQ ID NO:254)

Translation:

15 LDKKECTTNGEFCGISVFASFLCCSGLCVFVCI (SEQ ID NO:255)

Toxin Sequence:

20 Xaa1-Cys-Thr-Thr-Asn-Gly-Xaa1-Phe-Cys-Gly-Ile-Ser-Val-Phe-Ala-Ser-Phe-Leu-Cys-Cys-
Ser-Gly-Leu-Cys-Val-Phe-Val-Cys-Ile-^ (SEQ ID NO:256)

25 **Name:** R6.8
Species: radiatus
Isolated: No
Cloned: Yes

DNA Sequence:

30 ATTGGACAAGAGAAAATGCTTCCCAAAATCATTGGCTTGATGCT
GAACTACCTATGCTGCAGTGGCCGGTGTATTCTGCCTAGTTGAAC TGCCG
TGATGTCTTCTACTCCAT (SEQ ID NO:257)

35 **Translation:**

LDKRKCFPKNHFCGFVVMLNYLCCSGRCIFVCV (SEQ ID NO:258)

Toxin Sequence:

40 Lys-Cys-Phe-Xaa3-Lys-Asn-His-Phe-Cys-Gly-Phe-Val-Val-Met-Leu-Asn-Xaa5-Leu-Cys-Cys-
Ser-Gly-Arg-Cys-Ile-Phe-Val-Cys-Val-^ (SEQ ID NO:259)

45 **Name:** Rg6.5
Species: regius
Isolated: No

Cloned: Yes

DNA Sequence:

5 TTGAACAAGAGAAGCTGCCTCCTCTAGACTGGTTTGTGGCTTCATATAATTGGA
GCGTTCTGTGCTGTAGTGGCTACTGCCTGCGTCTGCATGTAAAAGTGCCTGAT
GTCTTCTCCTCCCCCTC (SEQ ID NO:260)

Translation:

10 LNKRSCLPLDWFCGFNIIGAFLCCSGYCLVVCM (SEQ ID NO:261)

Toxin Sequence:

15 Ser-Cys-Leu-Xaa3-Leu-Asp-Xaa4-Phe-Cys-Gly-Phe-Asn-Ile-Ile-Gly-Ala-Phe-Leu-Cys-Cys-
Ser-Gly-Xaa5-Cys-Leu-Val-Val-Cys-Met-^ (SEQ ID NO:262)

20 **Name:** De6.2
Species: delessertii
Isolated: No
Cloned: Yes

DNA Sequence:

25 ATGAAACTGACGTGTCTGCTGATCGTTGCTGTGCTGGTCTTGGCAGCCTGTCAGTTC
ATCGTAGCTGGCGACTCGAGTGATGGCCAGGAGAACCTGCTTGAGGTCACCTAG
CGATTCCCTCTGGGAAAATGTCATCAATGAAGCGCTCCAGACACGGCTGATGGTGG
GGCAATCTGCATCGAAAAGACCAAGCAAGAGGGACTGCATCCCCGGCGCGAAAAA
30 TTGTGATGTATTCCGACCATACCGGTGCTGCAGTGGATATTGCATACTACTCCTTTG
CGCATGATAAAGCTGCCTTGATGTCTTCTCCTCCCCCTC (SEQ ID NO:263)

Translation:

35 MKLTCLLIVAVLVLAACQFIVAGDSSDGQENPALRSPSDSSGKMSSMKRFQTRLMVGQ
SASKRPSKRDCIPGGENCDVFRPYRCCSGYCILLCA (SEQ ID NO:264)

Toxin Sequence:

40 Asp-Cys-Ile-Xaa3-Gly-Gly-Xaa1-Asn-Cys-Asp-Val-Phe-Arg-Xaa3-Xaa5-Arg-Cys-Cys-Ser-
Gly-Xaa5-Cys-Ile-Leu-Leu-Cys-Ala-^ (SEQ ID NO:265)

45 **Name:** Striat21
Species: striatus
Isolated: No
Cloned: Yes

DNA Sequence:

5 GCTGGTTCGCTGCAGGTACCGGTCCGGAATTCCGGGTCGACATCATCATCATCGA
 TCCATCTGTCCATCCATCTATTCAATTCAATTCTGCTGCCAAACTGTATTAAATATT
 CAAGTCTCTCTTCTGTTGTCTAACAGATTGAGATGGTGCATTCTAGTGGTGA
 ACTTTGTTCCGCTCGGATCACATAGGATGCTGCAGTGGCAAGTGCCTCGTCTG
 CTTGTAAAAGTGCCTGATGTCTCTCCTCCATCTAGTAGTAGTAGGCGGCCGCTC
 TAGAGGATCCAAGCTTACGTACCGTGCATGCGACGTACAGCTCTTCTATAGTGTG
 10 ACCTAAATTCAATTCAACTGGCCGTCGTTTACAACGTCGTGACTGGGAAAACCTGG
 CGTTACCCAACCTAATCGCCTTGCAGCACATCCCCCTTCGCCAGCTGGCGTAATAG
 CGAAGAGGCCCGCACCGATGCCCTCCAACAGTTGCGCAGCCTGAATGGCGAA
 TGGGACGCGCCCTGTAGCGGCCATTAAACCGCGGCCGGTGTGGGTGGGTTACGCC
 CACGTGACCCGCTACACTGCCAGCGCCCTANCGCCCGCTCCTTCGCTTCTTCC
 15 CTTCCCTTCTCGNCACGTTCGGCCGNTTTCCCCGTCAAGCTCTAAATGGGGGG
 CTTCCCTTAAGGGTTNCGAATTANTGCTTACCGGNACCCCTGACCCCCAAAAAA
 ACTTGGANTAAAGGGNGATGGNTNCCTGAANTGGGGGCCATNCCCCCTGAANAGA
 ACGGTTTTCNCCCCCTTGACNGTTGGGNTTCCNCGGTTTTAAAAAANGGGACC
 TTTNTTTCCAAAACGGAAANANACCTAAACCTATTGGGGCTATTGGGCTATTGGG
 20 TTTNAANGGGATTGGCCCATTTNGGCCNTTGGGTAAAAAAAGAGCCGG
 TTTAAAAAAATTTACCCAAATTAAACAAAAATTGGG (SEQ ID NO:266)

Translation:

25 LRWCIPSGELCFRSDHIGCCSGKCAFVCL (SEQ ID NO:267)

Toxin Sequence:

30 Leu-Arg-Xaa4-Cys-Ile-Xaa3-Ser-Gly-Xaa1-Leu-Cys-Phe-Arg-Ser-Asp-His-Ile-Gly-Cys-Cys-
 Ser-Gly-Lys-Cys-Ala-Phe-Val-Cys-Leu-^ (SEQ ID NO:268)

35 **Name:** 8Striatus 26
Species: striatus
Isolated: No
Cloned: Yes

DNA Sequence:

40 TTGAGATGGTGCATTCTAGTGGTATCTTGTGGCTCGGATCACATAGGATGC
 TGCAGTGGCAAGTGCCTGCTGCTTGAA (SEQ ID NO:269)

Translation:

45 LRWCIPSGDLCFRSDHIGCCSGKCAFVCL (SEQ ID NO:270)

Toxin Sequence:

Xaa4-Cys-Ile-Xaa3-Ser-Gly-Asp-Leu-Cys-Phe-Arg-Ser-Asp-His-Ile-Gly-Cys-Cys-Ser-Gly-Lys-Cys-Ala-Phe-Val-Cys-Leu-^ (SEQ ID NO:271)

5 **Name:** δStriatus 106
Species: striatus
Isolated: No
Cloned: Yes

10 **DNA Sequence:**

TTGAGATGGTGCATTCTAGTGGTATCTTGTTCCGCTCGGATCACATACAATGC
TGCAGTGGCAAGTGCGCATTCTGCTGTAA (SEQ ID NO:272)

15 **Translation:**

LRWCIPSGDLCFRSDHIQCCSGKCAFVCL (SEQ ID NO:273)

20 **Toxin Sequence:**

Xaa4-Cys-Ile-Xaa3-Ser-Gly-Asp-Leu-Cys-Phe-Arg-Ser-Asp-His-Ile-Gln-Cys-Cys-Ser-Gly-Lys-Cys-Ala-Phe-Val-Cys-Leu-^ (SEQ ID NO:274)

25 **Name:** O6.3
Species: obscurus
Isolated: No
Cloned: Yes

30 **DNA Sequence:**

cgatccatctgtccatccatccattcagtcattcgctgccaactgtaaacaaatattcaagtcttgctttctgtttgtctgacagATTGAG
ATGGTGCCTTCAGCGGTGAAGTTGTCGCCGCTATGAATTCTGGGATGCTGCAG
35 TGGCAAGTGCTCTTCGTCTGCTCGTAAAAGTGTGATGTCTTCCTCCCTC
(SEQ ID NO:275)

Translation:

40 VSDRLRWCVPSEVCRRYEFVGCCSGKCFVCS (SEQ ID NO:276)

Toxin Sequence:

Leu-Arg-Xaa4-Cys-Val-Xaa3-Ser-Gly-Xaa1-Val-Cys-Arg-Arg-Xaa5-Xaa1-Phe-Val-Gly-Cys-
45 Cys-Ser-Gly-Lys-Cys-Phe-Phe-Val-Cys-Ser-^ (SEQ ID NO:277)

Name: R6.3
Species: radiatus
Isolated: No
Cloned: Yes

5

DNA Sequence:

ctctctctctctgctggacaggTCGACTCGCTGCTGCCTGACGGAACGTCTGCCTTTAGTA
 GGATCAGATGCTGCGGTACTTGCAGTTCAATCTTAAAGTCATGTGTGAGCTGATCCG
 10 GCGGTTGATCTTCCTCCCTCTGTGCTCCATCCTTCTGCCTGAGTCCTCCTTACCTG
 AGAGTGGTCATGAACCACTCATCACCTACTCCTCTGGAGGCTTCAGAGGGAGCTACAT
 TGAAATAAAAGCCGCATTGC (SEQ ID NO:278)

10

Translation:

15

RSTRCLPDGTSLFSRIRCCGTSSILKSCVS (SEQ ID NO:279)

Toxin Sequence:

20

Cys-Leu-Xaa3-Asp-Gly-Thr-Ser-Cys-Leu-Phe-Ser-Arg-Ile-Arg-Cys-Cys-Gly-Thr-Cys-Ser-Ser-Ile-Leu-Lys-Ser-Cys-Val-Ser-^ (SEQ ID NO:280)

25

Name: G6.3
Species: geographus
Isolated: No
Cloned: Yes

DNA Sequence:

30

GGATCTTGCACGGTGAATTGCTTCATATTTCTACTGTCGTTGGCATCATCC
 AAAACATCACCAAGATGAAACTGACGTGCATGATGATCGTTGCTGTGCTGTTCTGA
 CCGCCTGGACATTGTCACGGCTGTGCCTCACTCCAGCGATGTATTGGAGAATCTT
 ATCTGAAGGCACTTACGAAACGGAAAACCACGAAGCCTCTAAATTGAACGTGAGA
 GACGACGAGTGCACCTCCTGGAGATTGGCTTTAAAATTGGGCCGCCT
 35 TGCTGCAGTGGCTGGTGCCTCTGGTGCCTAAACTGCCGTGATGTCTTCTATT
 CCCCTCTGTGCTACCTGGCTTGATCTTGATTGGCGCGTGCCTCAGGGTTATGAA
 CCCCCCTGAGCCGACTCTGGGGGCTCGGGGGTCAACATCCAAATAAGCGAC
 AACACAATCACAGTAAAAAA (SEQ ID NO:281)

40

Translation:

MKLCMMIVAVLFLTAWTFVTAVPHSSDVLENLYLKALHETENHEASKLNVRDDECEP
 PGDFCGFFKIGPPCCSGWCFLWCA (SEQ ID NO:282)

45

Toxin Sequence:

Asp-Asp-Xaa1-Cys-Xaa1-Xaa3-Xaa3-Gly-Asp-Phe-Cys-Gly-Phe-Phe-Lys-Ile-Gly-Xaa3-Xaa3-

Cys-Cys-Ser-Gly-Xaa4-Cys-Phe-Leu-Xaa4-Cys-Ala-[^] (SEQ ID NO:283)

5 **Name:** Tx6.8
Species: textile
Isolated: No
Cloned: Yes

DNA Sequence:

10 GCTGCAGGTCGACTCTAGAGGCCTGGAGAACCTTATCTGAAGGCACATCATGAA
ATGAACAAACCCGAAGACTCTGAATTGAACAAGAGGTGCTATGATAGTGGGACAAG
TTGTAACACTGGAAACCAATGCTGCAGTGGCTGGTGCATTTCTGCTGCCTCTAAAAA
CTGCCGTGATGTCTTCTACTCCCCTCTGTGCTACCTACCTGGCTGATCTTGATTGG
15 CGCGTGCCCTTCACTGGTTATGAACCCCTCTGATCCGACTCTCTGGGGCCTCGGGG
ATCCAACATCAAAATANAGCGACAGCACAATCAC (SEQ ID NO:284)

Translation:

20 CRSTLEALENLYLKAHHEMNNPEDSELNKRCYDSGTSCNTGNQCCSGWCIFVCL (SEQ
ID NO:285)

Toxin Sequence:

25 Cys-Xaa5-Asp-Ser-Gly-Thr-Ser-Cys-Asn-Thr-Gly-Asn-Gln-Cys-Cys-Ser-Gly-Xaa4-Cys-Ile-
Phe-Val-Cys-Leu-[^] (SEQ ID NO:286)

30 **Name:** Qc6.1
Species: quercinus
Isolated: No
Cloned: Yes

35 **DNA Sequence:**

GCTTCGTATTCCTCCGCTGTCTCCTTGGCATACCCAAAACATCACCAAGATGAAA
CTGACGTGCATGATGATCGTTGCTCTGCTGTTCTGACCGCCTGGACATTGTCACG
10 GCTGTTGACTCCAAAATGAACACTGGAGaACAGAGGAGGATGGGGCAGGCAGGAG
GATGGGGAAACTTTCCGATGGCACGCGACGAAATGAAAAACAGCGAAGTCTCT
AAATTGGACAATAAGAGAAAGTGCCTGCAGCCGGTAAGCTTGCCTAACTCTAT
CATTGGaAACGTATTTGCTGCAAAGGCTACTGtCTTTCTGCTGCATTAGTTAAACT
GcTGTGATGCCTTCTACTCACCTCTGTGCTACCTGGCTGATCTTGATTGGCGTGTGC
45 CCTTCACTGGTTATGAgCTCGTCTGAtCCTACTCTGGAGACCTCTGTGGTCCAACAt
CCaAATAAAAGCGGcATCCAAT (SEQ ID NO:287)

Translation:

MKLT CMMIV ALLFLTAWTFV TAVDSKNE LENRG GWGQAGG WGKL FPMAR DEMKNSE
VSKLDNKRKCAAAGEACV IIGNVFCCKGYCLFVCIS (SEQ ID NO:288)

5 **Toxin Sequence:**

Cys-Ala-Ala-Ala-Gly-Xaa1-Ala-Cys-Val-Ile-Xaa3-Ile-Ile-Gly-Asn-Val-Phe-Cys-Cys-Lys-Gly-
Xaa5-Cys-Leu-Phe-Val-Cys-Ile-Ser-^ (SEQ ID NO:289)

10 -----

15 **Name:** Lp6.5
Species: leopardus
Isolated: No
Cloned: Yes

DNA Sequence:

20 ATGAAACTGACGTGCGTGGTATCGTTGCTGTGCTGTTCTGACCGCCTGGATATT
ATCACGGCTGATGACTCCACAAATGGACTGGAGAATCGTTTAGGAAGGCACGTGA
CAACATGAAGAACGCCAAAGCCTCTACATTAGCCGAGAAGAAAGCGTGTGTTGAAC
TTGGTGAGATTGTGCCACAGGCTCTTCCTAGACGAGGAATGCTGCACTGGTTCAT
GCCATGTCTCTCGCTACTATAGTTAAACTGCTGTGATGTCTTCTCTCCCTCCGTG
CTACCTGGCTTGATCTTGATTGGTGCCTGTCCTCAGTGGTTGTGAAACCCTCTGAT
CCTACTCTCTGGACGCCCTGAGGCCAACATCCAAATAAGCGACATCCTAATGCC
AAAAAAAAAAAA (SEQ ID NO:290)

Translation:

30 MKLTCVVIVAVLFLTAWIFITADDSTNGLENRFRKARDNMKNAKASTLAEKKACVELG
EICATGFFLDEECCTGSCHVFCVL (SEQ ID NO:291)

Toxin Sequence:

35 Ala-Cys-Val-Xaa1-Leu-Gly-Xaa1-Ile-Cys-Ala-Thr-Gly-Phe-Phe-Leu-Asp-Xaa1-Xaa1-Cys-Cys-
Thr-Gly-Ser-Cys-His-Val-Phe-Cys-Val-Leu-^ (SEQ ID NO:292)

40 -----
Name: Mr6.4
Species: marmoreus
Isolated: No
Cloned: Yes

45 **DNA Sequence:**

ATGAAACTGACGTGCGTGGTATCGTTGCTGTGCTGTTCTGACCGCCTGGACATT

5 GCCACGGCTGATGACCCCAGAAATGGATTGGAGAATCTTTTCGAAGGCACATCA
 CGAAATGAAGAACCCCGAAGCCTCTAAATTGAACAAGAGGTGCCCTAACACTGGTG
 AATTATGTGATGTGGTTGAACAAAATGCTGCTATACCTATTGCTTATTGTAGTCT
 GCCTATAAAACTACCGTGATGTCTTACTCCCCCTGTGCTGCCTGGCTGATCTT
 GATTGGCGCGTGCCTCACTGGTTATGACCCCCCTGATCCGACCTCTGGGG (SEQ
 ID NO:293)

Translation:

10 MKLTCVVIVAVLFLTAWTFATADDPRNGLENLFSKAHHEMKNPEASKLNKRCPNTGEL
 CDVVEQNCCYTYCFIVVCL (SEQ ID NO:294)

Toxin Sequence:

15 Cys-Xaa3-Asn-Thr-Gly-Xaa1-Leu-Cys-Asp-Val-Val-Xaa1-Gln-Asn-Cys-Cys-Xaa5-Thr-Xaa5-
 Cys-Phe-Ile-Val-Val-Cys-Leu-^ (SEQ ID NO:295)

20 **Name:** Qc6.2
Species: quercinus
Isolated: No
Cloned: Yes

DNA Sequence:

25 GGATCCATGAAACTGACGTGTATGGTATCGTTGCTGTGCTATTCTGACCGCCTCG
 GCTGATGACTCCAGAAATGGATTGAGAATCGAAATGGAGAACGAAACGAAAACG
 AAATGAAGAACCTCGAACGCTCTAAATTGAACAGGAGAGACGGCGATTGCGTTGAT
 30 GGTGGTGAATTGTGGCTTCCGAAAATTGGAGGGCCATGCTGTAGTGGCTGGTC
 TTTTCGTCTGCTTATAAAACTGCCATGATGTCTTCTACCCCCCTGTGCTACCTGA
 CTTGATCTTGATTGGCGTGTGCCCTCACTGGTTATGAACCCCTGTGATCCGACTCT
 CTGGAGGCCTGGGGTCCAACATCCAAATAAGCGACAGCAAAAAAAAAAAAAAA
 AAAAAAA (SEQ ID NO:296)

Translation:

35 MKLTCMVIVAVLFLTASADDSRNGFENRNGERNENEMKNLEASKLNRRDGDCVDGGE
 FCGFPKIGGPCCSGWCFFVCL (SEQ ID NO:297)

40 **Toxin Sequence:**
 45 Asp-Gly-Asp-Cys-Val-Asp-Gly-Gly-Xaa1-Phe-Cys-Gly-Phe-Xaa3-Lys-Ile-Gly-Gly-Xaa3-Cys-
 Cys-Ser-Gly-Xaa4-Cys-Phe-Phe-Val-Cys-Leu-^ (SEQ ID NO:298)

Name: Qc6.3
Species: quercinus
Isolated: No
Cloned: Yes

5

DNA Sequence:

GGATCCATGAAACTGACGTGCGTGGTATCGTTGCTGTGCTATTCTGACCGCCTTG
 GCTGATGACTCCAGAAATGGATTGGAGAATCGAAATGAACAAGAACGAAACGAAA
 10 ACGAAATGAGGGACCGCCGGACTGCCAAGATAGTGGTAGTTGTGGCTTCCG
 AACACCTGAACCACACTGCTGCAGTGGCTGGCTTCTGCGCCTAAACTGC
 CGTATGTCAAATAAAGCGACAGACAATNAAAAAAA (SEQ ID
 NO:299)

15

Translation:

MKLTCVVIVAVLFLTALADDSRNGLENRNEQERNENEMDRRDCQDSGVVCGFPKPEP
 HCCSGWCLFVCA (SEQ ID NO:300)

20

Toxin Sequence:

Asp-Cys-Gln-Asp-Ser-Gly-Val-Val-Cys-Gly-Phe-Xaa3-Lys-Xaa3-Xaa1-Xaa3-His-Cys-Cys-
 Ser-Gly-Xaa4-Cys-Leu-Phe-Val-Cys-Ala-^ (SEQ ID NO:301)

25

Name: Ar6.5
Species: arenatus
Isolated: No
 30 **Cloned:** Yes

DNA Sequence:

GGATCCATGAAACTGACGTGTTGGTATCGTTGCTGTGCTATTCTGACCGCCTGG
 35 ACATTCTACGGCTGACTCCATACGTGCACTGGAGGATTTTGCAGGACACGT
 GACGAAATGGAAAACAGCGGAGCTTCTCCATTGAACGAGAGAGACTGCCGACCTGT
 AGGTCAATATTGTGGCATACCGTATAAGCACAACGGCGATGCTGCAGTCAGCTTG
 TGCAATTATCTGTGTTCTAACCCCTCTGATCCTACTCTGAAGACCTCCGGGATT
 40 CAACATCCAAATAAAGCGACATCCGATNAAAAAANGAAAAAAA (SEQ ID NO:302)

45

Translation:

MKLTCVVIVAVLFLTAWTFVTADSIRALEDFFAKARDEMENSGASPLNERDCRPVGQY
 45 CGIPYKHNWRCCSQLCAIICVS (SEQ ID NO:303)

Toxin Sequence:

Asp-Cys-Arg-Xaa3-Val-Gly-Gln-Xaa5-Cys-Gly-Ile-Xaa3-Xaa5-Lys-His-Asn-Xaa4-Arg-Cys-Cys-Ser-Gln-Leu-Cys-Ala-Ile-Ile-Cys-Val-Ser-^ (SEQ ID NO:304)

5 -----

10 **Name:** Ar6.11
Species: arenatus
Isolated: No
Cloned: Yes

DNA Sequence:

15 GGATCCATGAAACTGACGTGTGGTATCGTTGCTGTTCTTGACCGCCTGG
ACATTCTCAAGGCTGATGACTCCATAAATGGATTGGAGAATCTTTCCGAAGGCA
CGTCACGAAATGAAGAACCCGAAGCCTCTAAATTGAACGAGAGGTGCCTGAAAAA
GGGTGTACTTGTGATCCGAGTGCTGGAAACTGCTGTAGTGGCGAATGCGTTTAGT
CTGCCTCTAAACTACCGTGATGTCTTACTCCCATCTGTGCTACCCCTCGAG (SEQ
ID NO:305)

20 **Translation:**

MKLTCVVIVVVLFLTAWTFVKADDSINGLENLFPKARHEMKNPEASKLNERCLEKGVL
CDPSAGNCCSGECVLVCL (SEQ ID NO:306)

25 **Toxin Sequence:**

Cys-Leu-Xaa1-Lys-Gly-Val-Leu-Cys-Asp-Xaa3-Ser-Ala-Gly-Asn-Cys-Cys-Ser-Gly-Xaa1-Cys-
Val-Leu-Val-Cys-Leu-^ (SEQ ID NO:307)

30 -----

35 **Name:** Ar6.12
Species: arenatus
Isolated: No
Cloned: Yes

DNA Sequence:

40 GGATCCATGAAACTGACGTGCATGGTATCGTTACTGTGTTGCTTGACCGCCTGG
ACATTCTCACGGCTGATGACTCCAGAAATGAATTGGAGAATCTTTCTGAAGGCA
TATCACGAAATGAACCTCGAACGCCTCTAAATTGGACAAGAAAGAGTGCCTGCTGG
TAGTCACTTTGTGGTTCCGAAAATTGGAGGGCCATGCTGCAGTGGCTGGTCTT
TTTCGTCTGCTGTAAACCTGCCGTATGTCTTACTCCCATCTGTGCTACCCCTCG
45 AG (SEQ ID NO:308)

Translation:

MKLTCMVIVTFLTAWTFVTADDSRNELENLFLKAYHEMNSEASKLDKKECVAGSHF
CGFPKIGGPCCSGWCFVCL (SEQ ID NO:309)

5 **Toxin Sequence:**

Xaa1-Cys-Val-Ala-Gly-Ser-His-Phe-Cys-Gly-Phe-Xaa3-Lys-Ile-Gly-Gly-Xaa3-Cys-Cys-Ser-
Gly-Xaa4-Cys-Phe-Phe-Val-Cys-Leu-^ (SEQ ID NO:310)

10 -----

15 **Name:** Ts6.2
Species: tessulatus
Isolated: No
Cloned: Yes

DNA Sequence:

20 GGATCCATGAAACTGACGTGTGGTATCGTTGCTGTGATGTTCTTGACCGCCTGG
 ACATTCATCACGGCTGATGACTCCATAAAATGGACTGGAGGATAGAGGCATATGGGG
 GGAACCTTGTGAGGCACGTGACGAAATGAACCCCGAAGTCTCTAAACGGGATT
 GCTGGCCTCAATATTGGTTTGTGGCCTACAGAGGGGATGCTGCCAGGGACTACTT
 GCTTCTCCTTGCTTTAGTGAATCTCGACTCCCTCTGTGCTACCTGGCTTGACC
 TTTGATTGGCGCGTGCCTCACTGGTTATAAACCCCTGTTCCTCCTCTGGACG
 25 CTTGGGGTGTCCAGCATCCAAATAAGCGACGTCCCCAAAAAAAAAAAAAA
 AA (SEQ ID NO:311)

Translation:

30 MKLTCVVIVAVMFLTAWTFITADDSINGLEDRGIWGEPLSKARDEMNP
 EVSKRDCWPQ YWFCGLQRGCCPGTTCFFLCF (SEQ ID NO:312)

Toxin Sequence:

35 Asp-Cys-Xaa4-Xaa3-Gln-Xaa5-Xaa4-Phe-Cys-Gly-Leu-Gln-Arg-Gly-Cys-Cys-Xaa3-Gly-Thr-
 Thr-Cys-Phe-Phe-Leu-Cys-Phe-^ (SEQ ID NO:313)

40 **Name:** Ts6.4
Species: tessulatus
Isolated: No
Cloned: Yes

45 **DNA Sequence:**

GGATCCATGAAACTGACGTGCGTGGTGGTCGGTGTGCTGTTCTGAACGCCTGG

5 ACATTGCCACGGCTGTTGACTCCAAACATGCACTGGCGAAACTTTTATGAAGGCA
 CGTGACGAAATGTATAACCCCGATGCCACTAAATTGGACGATAAGAGATGGTGC
 TTAGATGGTGAACCTTGATCATACCGGTCAATTGGTCCATATTTGCTGCCATGGC
 ATATGTATGATCTACTGCGTCTAGTTGAACTGCCGTGATGTCTTACTCCCCTGT
 GCTACCCCTGGTTGATCTTGATTGCCCTGTGCCCTCACTGATTATGAATCCCTCT
 GATCCTACTCTGAAGACCTCTGGGGTCCAACATCCAAATAAAGCGACATCCCAA
 AAAAAAAAAAAAAAAA (SEQ ID NO:314)

Translation:

10 MKLTCVVVAVLFLNAWTFATAVDSKHALAKLFMKARDEMNPDATKLDDKRWCA
 LDGELECIIPVIGSIFCCHGICMIYCV (SEQ ID NO:315)

Toxin Sequence:

15 Xaa4-Cys-Ala-Leu-Asp-Gly-Xaa1-Leu-Cys-Ile-Ile-Xaa3-Val-Ile-Gly-Ser-Ile-Phe-Cys-Cys-His-
 Gly-Ile-Cys-Met-Ile-Xaa5-Cys-Val-^ (SEQ ID NO:316)

20 -----

Name: Im6.1
Species: imperialis
Isolated: No
Cloned: Yes

25 **DNA Sequence:**

GGATCCATGAAACTGACGTGCGTGGTTCGTTGCTGTGCCGTTCTGACCGCCTCG
 GTATTCATCACGGCTGATGACTCCAGAAATGGAATCGAGAATCTCCTCGGATGAG
 30 ACGTCACGAAATGAAGAACCCCAAAGCCTCTAAGTTGAACAAAGAGACAGTGCCGTG
 TAGAAGGTGAAATTGTCGGCATGCTGTTGAAGCACAATGCTGCGATGGCTGGTGC
 TTTTCGTCATGTAAGACTGCCGTGATGTCTTACTCTCCTCTGTGCTACCTGCC
 CTGATCTTGATTGGCTCGCGCCCTCATTGGTTATGAACCCCTGTGATCCTACTCTC
 TGGAGGCCTCAGGGTCCAGCATCTAAATAAAGCGACATCACAATCAAAAAAAA
 35 AAAAAAAAAA (SEQ ID NO:317)

Translation:

MKLTCVVFVAVPFLTASVFITADDSRNGIENLPRMRRHEMKNPKASKLNKRQCRVEGEI
 10 CGMLFEAQCCDGWCFVCM (SEQ ID NO:318)

Toxin Sequence:

Xaa2-Cys-Arg-Val-Xaa1-Gly-Xaa1-Ile-Cys-Gly-Met-Leu-Phe-Xaa1-Ala-Gln-Cys-Cys-Asp-
 15 Gly-Xaa4-Cys-Phe-Phe-Val-Cys-Met-^ (SEQ ID NO:319)

5 **Name:** Ca6.5
Species: characteristicus
Isolated: No
Cloned: Yes

DNA Sequence:

10 GGATCCATGAAACTGACGTGTGGTATCGTTGCTGTGCTGTTCTTGACCGCCTGG
ACATTCGTCACGGCTGATGACTCCAGAAATGGATTGGAGAATCTTTCCGAAGGCA
CGTCACGAAATGAAGAACCCCGAAGCCTCTAAATTGAACAAGAGGTGCGTTGACCC
TGGTGAATTGTGGTCCGGGATTGGAGATTGCTGCAGTGGCTCTGCCTTTAGTC
TGCATCTAAAAGTGCCTGATGTCTTACTCCATCTGTGCTACCCCTCGAG (SEQ
15 ID NO:320)

Translation:

20 MKLTCVVIVAVLFLTAWTFVTADDNRNGLENLFPKARHEMKNPEASKLNKRCVDPGEF
CGPGFGDCCTGFCLLVCI (SEQ ID NO:321)

Toxin Sequence:

25 Cys-Val-Asp-Xaa3-Gly-Xaa1-Phe-Cys-Gly-Xaa3-Gly-Phe-Gly-Asp-Cys-Cys-Thr-Gly-Phe-Cys-
Leu-Leu-Val-Cys-Ile-^ (SEQ ID NO:322)

30 **Name:** Mf6.2
Species: miliaris
Isolated: No
Cloned: Yes

DNA Sequence:

35 GGATCCATGAAACTGACGTGCGTGGTATCGTTGCTGTGTTCTTGACCGCCTGG
ACATTCGTCATGGCTGATGACTCCAGAAATGATTGGAGAATCTTTCTGAAGGCA
CGTCATGAAATGAAGAACCCCGAAGCTTCTAAATTGAACAAGAGATGCCTCCAAA
TGGTGTACTTGTGATCTGGGATCTCCACCATACTGCTGCAGTGGCTGGTGCAGCGAT
10 CGTCGTCTGCATCTAAAAGTGCCTGATGTCTTACTCCATCTGTGCTACCCCTCG
AG (SEQ ID NO:323)

Translation:

15 MKLTCVVIVAVLFLTAWTFVMADDNRNDLENLFLKARHEMKNPEASKLNKRCCLPNGV
LCDLGSPPYCCSGWCAIVVCI (SEQ ID NO:324)

Toxin Sequence:

Cys-Leu-Xaa3-Asn-Gly-Val-Leu-Cys-Asp-Leu-Gly-Ser-Xaa3-Xaa3-Xaa5-Cys-Cys-Ser-Gly-Xaa4-Cys-Ala-Ile-Val-Val-Cys-Ile-^ (SEQ ID NO:325)

5

Name: Ak6.1
Species: atlanticus
Isolated: No
Cloned: Yes

DNA Sequence:

15 GGATCCATGAAACTGACGTGCGTGGTATCGTTGCTGTGCTGTTCTGACCGCCTGG
 ACATTCGTCACGGCTGATGACTCCATAAATGGGTTGGAGAATCTTTTCCGAAGGCA
 CGTCACGAAATGAGGAAACCCGAAGCCTCTAGATCGAGAGGGAGGTGCCGTCTCG
 TGGTATGTTCTGTGGCTTCCGAAACCTGGACCATACTGCTGCAATGGCTGGTGCTT
 TTTCGTCTGCATCTAAACTGCCGTGATGTGTTACTCCCATCTGTGCTACCCCTCG
 20 AG (SEQ ID NO:326)

Translation:

25 MKLTCVVIVAVLFLTAWTFVTADD SINGLENLPKARHEMRKPEASRSRGCRPRGMF
 CGFPKPGPYCCNGWCFFVCI (SEQ ID NO:327)

Toxin Sequence:

30 Cys-Arg-Xaa3-Arg-Gly-Met-Phe-Cys-Gly-Phe-Xaa3-Lys-Xaa3-Gly-Xaa3-Xaa5-Cys-Cys-Asn-
 Gly-Xaa4-Cys-Phe-Phe-Val-Cys-Ile-^ (SEQ ID NO:328)

35 **Name:** Lv6.1
Species: lividus
Isolated: No
Cloned: Yes

DNA Sequence:

40 GGATCCATGAAACTGACGTGCGTGGTATCGTTGCTGTGCTGTTCTGACCGCCTGG
 ACATTGCCACGGCTGATGACCCCAGAAATGGATTGGAGAATCTTTTTCGAAGGCA
 CATCACGAAATGAAGAACCCCGAAGCCTCTAAATTGAACAAAGAGGTGCCCTAACAC
 TGGTGAATTATGTGATGTGGTTGAACAAAACTGCTGCTATAACCTATTGCTTATTGT
 45 AGTCTGCCTATAAAACTACCGTATCTCTTACTCCCATCTGTGCTACCCCTCGAG
 (SEQ ID NO:329)

Translation:

MKLTCVVIVAVLFLTAWTFATADDPRNGLENLFSKAHHEMKNPEASKLNKRCPNTGEL
 CDVVEQNCCYTYCFIVVCL (SEQ ID NO:330)

5

Toxin Sequence:

Cys-Xaa3-Asn-Thr-Gly-Xaa1-Leu-Cys-Asp-Val-Val-Xaa1-Gln-Asn-Cys-Cys-Xaa5-Thr-Xaa5-
 Cys-Phe-Ile-Val-Val-Cys-Leu-^ (SEQ ID NO:331)

10

Name: Pu6.3
Species: pulicarius
Isolated: No
Cloned: Yes

DNA Sequence:

20 GGATCCATGAAACTGACGTGCATGGTATCGTGCTGCTGCTTCTGACCGCCTGG
 ACATTCGTCAAGGCTGATGACTCCAGAAATGGATTGGAGAATCTTTTCCGAAGGC
 ACGTCACGAAATGAAGAACTCCAAAGCCTCTAAATTAAACAAGAGGTGCGTTGAAG
 ATGGTGATTTGTGGTCCGGGATATGAAGAGTGCTGCAGTGGCTTCTGCCTTACG
 TCTGCATCTAAAAGTCCGTGATGTCTTACTCCCATCTGTGCTACCCCTCGAG
 (SEQ ID NO:332)

Translation:

MKLTCMVIVAVLFLTAWTFVKADDNRNGLENLFPKARHEMKNASKLNKRCVEDGD
 30 FCGPGYEECCSGFCLYVCI (SEQ ID NO:333)

Toxin Sequence:

Cys-Val-Xaa1-Asp-Gly-Asp-Phe-Cys-Gly-Xaa3-Gly-Xaa5-Xaa1-Xaa1-Cys-Cys-Ser-Gly-Phe-
 35 Cys-Leu-Xaa5-Val-Cys-Ile-^ (SEQ ID NO:334)

Name: Ge6.1
Species: generalis
Isolated: No
Cloned: Yes

DNA Sequence:

45 GGATCCATGAAACTGACGTGTGGTATCGTGCTGCTATTCTGACCGCCTGG
 ACATTCGTACGGCTGATGACACCAGATATAACTGGAGAATCCTTTCTGAAGGC

ACGCAACGAAC TG CAGAAACACGAAGCCTCTCAACTGAACGAGAGAGGCTGCCTTG
 ACCCAGGTTACTTCTGTGGGACGCCGTTCTTGGAGCATACTGCTGCAGTGGCATT
 GCCTTATTGTCTGCATAGAAACGTAAAGGCTTGATGTCTTCTACTCCCATCTGTGCT
 ACCCCTCGAG (SEQ ID NO:335)

5

Translation:

MKLTCVVIVAVLFLTAWTFVTADDTRYKLENPFLKARNEHQHEASQLNERGCLDPGY
 FCGTPFLGAYCCGGICLIVCIET (SEQ ID NO:336)

10

Toxin Sequence:

Gly-Cys-Leu-Asp-Xaa3-Gly-Xaa5-Phe-Cys-Gly-Thr-Xaa3-Phe-Leu-Gly-Ala-Xaa5-Cys-Cys-
 Gly-Gly-Ile-Cys-Leu-Ile-Val-Cys-Ile-Xaa1-Thr-^ (SEQ ID NO:337)

15

Name: Ep6.1
Species: episcopatus
Isolated: No
Cloned: Yes

DNA Sequence:

GGATCCATGAAACTGACGTGCGTGGTATCGTTGCTGTGCTGTTCTGACCGCCTGG
 ACATTTGCCACGGCTGATGACCCAGAAATGGATTGGGAATCTTTTCGAATGTA
 CATCACGAAATGAAGAACCTCGAAGACTCTAAATTGGACAAGAAGTGCCTGGTT
 TGGTGAAGCTTGTCTTATGCTTATTCAAGACTGCTGCAGCTATTGCGTTGCTCTGTC
 TGCCTATAAAACTACCGTGACGTCTACTCCCTCTGTGCTACCTGGCTTGATCTT
 30 TGATTGGCGTGTGCGCTTCACTGGTTATGAACCCCTGTGATCCTACTCTGAAGAC
 CTCTGGGGTCCAACATCCAAATAAGCGACATCACAAAAAAA
 AA (SEQ ID NO:338)

25

Translation:

MKLTCVVIVAVLFLTAWTFATADDPRNGLGNLFSNVHHEMKNLEDSKLDKKCLGFGE
 ACLMLYSDCCSYCVALVCL (SEQ ID NO:339)

35

Toxin Sequence:

10 Cys-Leu-Gly-Phe-Gly-Xaa1-Ala-Cys-Leu-Met-Leu-Xaa5-Ser-Asp-Cys-Ser-Xaa5-Cys-Val-
 Ala-Leu-Val-Cys-Leu-^ (SEQ ID NO:340)

45

Name: Ep6.2
Species: episcopatus

Isolated: No
Cloned: Yes

DNA Sequence:

5 GGATCCATGAAACTGACGTGCGTGGTGATCATTGCTGTGCTGTTCTGACCGCCTGG
 ACATTCGTCATGGCTGATGACCCCAGAGATGAACCGGAGGCACGTGACGAAATGAA
 CCCCGCAGCCTCTAAATTGAACCGAGAGAGGCTGCCTGCAGTTGATTATTTTGC
 GGC
10 CATACCGTTTGTGAGCAACGGGCTATGCTGCAGTGGCAATTGTGTTTGCTGCAC
 ACCCCAAGGGAAGTAAAAGTGCCTGACGTCTCTACTCCCCTCTGTGCTACCTGGC
 TTGATCTTGATTGGCGTGTGCACTTCACTGGTTATGAACCCCTCTGATCCTACTCTC
 TGAAGACCTCTGGGTCCAACATCCAAATAAGCGACATCCAAAAAAA
 AAAAAAA (SEQ ID NO:341)

15 **Translation:**

MKLTCVIIIAVLFLTAWTFVMADDPRDEPEARDEMNPAAASKLNERGCLAVDYFCGIPF
 VSNGLCCSGNCVVFVCTPQGK (SEQ ID NO:342)

20 **Toxin Sequence:**

Gly-Cys-Leu-Ala-Val-Asp-Xaa5-Phe-Cys-Gly-Ile-Xaa3-Phe-Val-Ser-Asn-Gly-Leu-Cys-Cys-
 Ser-Gly-Asn-Cys-Val-Phe-Val-Cys-Thr-Xaa3-Gln-# (SEQ ID NO:343)

25 -----

Name: Ac6.1
Species: achatinus
Isolated: No
30 **Cloned:** Yes

DNA Sequence:

35 CGATCCTCTGCTCCATCTATTATTATTCGCTGCCAAACTGTGTTAAATATTCAAGT
 CTCTCTTCTGTTGTCTAACAGGTTGAGATGGTGCATTCTAGAGGTGATCTTG
 TTTCCCCCTCGGATCGCATACAATGCTGCAGTGGCAAGTGCACATTGCTCTGCATGTA
 AAACTGCCGTGATGTCTTCCTCCCTC (SEQ ID NO:344)

Translation:

40 LRWCIPRGDLCFPSDRIQCCSGKCTFVCM (SEQ ID NO:345)

Toxin Sequence:

45 Xaa4-Cys-Ile-Xaa3-Arg-Gly-Asp-Leu-Cys-Phe-Xaa3-Ser-Asp-Arg-Ile-Gln-Cys-Cys-Ser-Gly-
 Lys-Cys-Thr-Phe-Val-Cys-Met-^ (SEQ ID NO:346)

5 **Name:** Ac6.2
Species: achatinus
Isolated: No
Cloned: Yes

DNA Sequence:

10 CGATCCTCTGTCCCTCCTCATTCAATCGCTGCCAAACTGTATTAAATATTGAAT
CTCTCTTCTGTTGTCTGACAGATTGAGAGGGTGCCTAGTGGTGAATTTG
TTACTTCATGGATCACATAGGATGCTGCAGTGGCAAGTGCACATTGCTCTGCATGTA
AAACTGCCGTGATGTCTCCTCCCATC (SEQ ID NO:347)

15 **Translation:**

LRGCVPSGEICYFMDHIGCCSGKCTFVCM (SEQ ID NO:348)

Toxin Sequence:

20 Gly-Cys-Val-Xaa3-Ser-Gly-Xaa1-Ile-Cys-Xaa5-Phe-Met-Asp-His-Ile-Gly-Cys-Cys-Ser-Gly-
Lys-Cys-Thr-Phe-Val-Cys-Met-^ (SEQ ID NO:349)

25 **Name:** Bu6.7
Species: bullatus
Isolated: No
Cloned: Yes

30 **DNA Sequence:**

35 ATGAAACTGACGTGCGTGATGATCGTTACTGTGCTGTTGACCGCCTGGACATTG
GTCACGGCTGATGACTCCACATATGGATTGAAGAATCTTGCCGAACGGACGTCAT
GAAATGATGAACCCCGAAGCCCCCTAAATTGAACAAGAAAGATGAATGCTCTGCTCC
TGGTGCATTTGTCTCATCAGGCCAGGACTCTGCTGCAGCGAGTTCTGCTTCTTGCG
TGTTTTAGTGACGGTTGATGTCTTACTCCCCCTC (SEQ ID NO:350)

Translation:

40 MKLTCVMIVVLFLTAWTFVTADDSTYGLKNLLPNGRHEMMNPEAPKLNKKDECSAP
GAFCLIRPGLCCSEFCFFACF (SEQ ID NO:351)

Toxin Sequence:

45 Asp-Xaa1-Cys-Ser-Ala-Xaa3-Gly-Ala-Phe-Cys-Leu-Ile-Arg-Xaa3-Gly-Leu-Cys-Cys-Ser-Xaa1-
Phe-Cys-Phe-Phe-Ala-Cys-Phe-^ (SEQ ID NO:352)

5 **Name:** Bu6.8
Species: bullatus
Isolated: No
Cloned: Yes

DNA Sequence:

10 ATGAAACTGACGTGCGTGATGATCGTTACTGTGCTGTTCTGACCGCCTGGACATTG
 GTCACGGCTGATGACTCCAGAGACGCTCCGGATAGTCAGAAGGATGGGAGAAACT
 TTTCTCGGAGGCACGTGACGAAATGAAGAACCGCAAAGACTTGAATTGAGAGGGT
 GCCTTCCTAGGTGGGAATTTGTCATCTTAAAAAAACGATTGCTGCAGTGGCA
15 TATGCATAAGCATCTGCTTGTAAAACCCGTGATGTCTTCTTCCCATC (SEQ ID
 NO:353)

Translation:

20 MKLTCVMIVTVLFLTAWTFVTADDSDAPDSAEGWEKLFSEARDEMKNRKDFELRGC
 LPRWEFCPIFKKNDCCSGICISICL (SEQ ID NO:354)

Toxin Sequence:

25 Gly-Cys-Leu-Xaa3-Arg-Xaa4-Xaa1-Phe-Cys-Xaa3-Ile-Phe-Lys-Lys-Asn-Asp-Cys-Cys-Ser-
 Gly-Ile-Cys-Ile-Ser-Ile-Cys-Leu-^ (SEQ ID NO:355)

30 **Name:** Sx6.4
Species: striolatus
Isolated: No
Cloned: Yes

35 **DNA Sequence:**

ATGAAACTGACGTGCATGATGATTGTTGCTGTGCTGTTCTGACCGCCTGGATATT
 GTAATGGCTGATGACTCCAGAAATGGATTGGAGAAATCTTCCTCAGACTACACGTCA
 CGAAATGAAGAACCCCGAAGCCTCTAAATTGAACCAGACAGACTGCCTTGCTAAAG
10 ACGCTTTCTGTGCCTGGCCGATACTTGGACCCTGTGCTGCAGTCGCTTGTGCTTAT
 ACGTCTGCATGtaaAACTGCCGTGATGTCTTCTACTCCCCTC (SEQ ID NO:356)

Translation:

15 MKLTCMMIVAVLFLTAWIFVMADDSRNG^ ENLPQTTRHEMKNPEASKLNQTDCLAKD
 AFCAWPILGPLCCSRLCLYVCM (SEQ ID NO:357)

Toxin Sequence:

Asp-Cys-Leu-Ala-Lys-Asp-Ala-Phe-Cys-Ala-Xaa4-Xaa3-Ile-Leu-Gly-Xaa3-Leu-Cys-Cys-Ser-Arg-Leu-Cys-Leu-Xaa5-Val-Cys-Met-^ (SEQ ID NO:358)

5

Name: Cn6.9
Species: consors
Isolated: No
Cloned: Yes

10

DNA Sequence:

15 ATGAAACTGACGTGCATGATGATCGTTGCTGTGCTGTTCTGACCGCCTGGACATTGTCACGGCTGATGACTCCAGAAATGGATTGGAGAATCTTCTCGAAGGCACGTCA
 CGAAATGAAGAACCCCGAAGCCTCTAAATCGAACAAAGAGATATGAGTGCTATTCTA
 CTGGTACATTTGTGGCATCACGGAGGACTCTGCTGCAGCAACCTTGCTTATTCTA
 CGTGTGCTTAACATTTCGTATGTCTTCTCCTCCCCTC (SEQ ID NO:359)

20

Translation:

MKLT CMMIVAVLFLTAWTFVTADD SRNGLENLSPKARHEMKNPEASKSNKRYECYST
 GTFCGINGGLCCSNLCLFFVCLTFS (SEQ ID NO:360)

25

Toxin Sequence:

Xaa5-Xaa1-Cys-Xaa5-Ser-Thr-Gly-Thr-Phe-Cys-Gly-Ile-Asn-Gly-Gly-Leu-Cys-Cys-Ser-Asn-Leu-Cys-Leu-Phe-Phe-Val-Cys-Leu-Thr-Phe-Ser-^ (SEQ ID NO:361)

30

35

Name: Cn6.10
Species: consors
Isolated: No
Cloned: Yes

DNA Sequence:

40 ATGAAACTGACGTGCCTGATGATCGTTGCTGTGCTGTTCTGACCA CCTGGACATTGTCACGGCTGATGACTCCAGATATGGATTGAAGAATCTTTCCGAAGGCACGTCA
 GAAATGAAGAACCCCTGAAGCCTCTAAATTGAACAAGAGAGATGGGTGCTATAATGC
 TGGTACATTTGTGGCATCCGTCCAGGACTCTGCTGCAGCGAGTTGCTTTATGG
 TGCATAAACATTGTTGATTCTGGCTAACAGTGTGCGTTGGTTGATGTCTTCTACTCCC
 45 CTC (SEQ ID NO:362)

Translation:

MKLTCLMIVAVLFLTTWTFVTADDsRYGLKNLFPKARHEMKNPEASKLNKRDGCYNA
GTFCGIRPGLCCSEFCFLWCITFVDSG (SEQ ID NO:363)

5 **Toxin Sequence:**

Asp-Gly-Cys-Xaa5-Asn-Ala-Gly-Thr-Phe-Cys-Gly-Ile-Arg-Xaa3-Gly-Leu-Cys-Cys-Ser-Xaa1-
Phe-Cys-Phe-Leu-Xaa4-Cys-Ile-Thr-Phe-Val-Asp-Ser-# (SEQ ID NO:364)

10 -----

15 **Name:** Cr6.6
Species: circumcisus
Isolated: No
Cloned: Yes

DNA Sequence:

20 CGATCCATCTGTCCATCCATCTATTCAATTCTCGCTGCCAAACTGTATTAAATATT
AAGTCTCTCTTCTGTTGTCTAACAGATTGAGTAGGTGCATTCTAGTGGTGATC
TTTGTTCCTCGGATCACATACAATGCTGCAATGCCAAGTGCAGCATTGCTCTGCTT
GTAAAAGTGCCGTGATGTCTTCTCTCCCTC (SEQ ID NO:365)

25 **Translation:**

NRLSRCIPSGDLCFPSDHIQCCNAKCAFVCL (SEQ ID NO:366)

Toxin Sequence:

30 Cys-Ile-Xaa3-Ser-Gly-Asp-Leu-Cys-Phe-Xaa3-Ser-Asp-His-Ile-Gln-Cys-Cys-Asn-Ala-Lys-
Cys-Ala-Phe-Val-Cys-Leu-^ (SEQ ID NO:367)

35 **Name:** Cr6.5
Species: circumcisus
Isolated: No
Cloned: Yes

40 **DNA Sequence:**

CGATCCATCTGTCCATCCATCTATTCAATTCTCGCTGTCAAACGTATTAAATATT
AAGTCTCTCTTCTGTTGTCTAACAGATTGAGTAGGTGCATTCTAGTGGTGATC
TTTGTTCCTCGGATCACATACAATGCTGCAAGTGCAGCATTGCTCTGCTT
GTAAAAGTGCCGTGATGTCTTCTACTCCCTC (SEQ ID NO:368)

Translation:

NRLSWCIPSGDLCFPSDHIQCCSAKCAFVCL (SEQ ID NO:369)

Toxin Sequence:

5 Xaa4-Cys-Ile-Xaa3-Ser-Gly-Asp-Leu-Cys-Phe-Xaa3-Ser-Asp-His-Ile-Gln-Cys-Cys-Ser-Ala-Lys-Cys-Ala-Phe-Val-Cys-Leu-^ (SEQ ID NO:370)

10

Name: Cr6.5A
Species: circumcisus
Isolated: No
Cloned: Yes

15

DNA Sequence:

20 CGATCCATCTGTCCATCCATCTATTCAATTCAATTGCTGTCAAACGTATTAAATATTCAAGTCTCTCTTCTGTTGTCTAACAGATTGAGTAGGTGCATTCTAGTGGTGATCTTGTTCCTCGGATCACATACAATGCTGCAGTGCCAAGTGCAGCATTCTGCTGTAAACTGCCGTATGTCTTCTCCTCCCCTC (SEQ ID NO:371)

Translation:

25

NRLSRCIPSGDLCFPSDHIQCCSAKCAFVCL (SEQ ID NO:372)

Toxin Sequence:

30

Cys-Ile-Xaa3-Ser-Gly-Asp-Leu-Cys-Phe-Xaa3-Ser-Asp-His-Ile-Gln-Cys-Cys-Ser-Ala-Lys-Cys-Ala-Phe-Val-Cys-Leu-^ (SEQ ID NO:373)

35 -----
Name: Cr6.6A
Species: circumcisus
Isolated: No
Cloned: Yes

40

DNA Sequence:

45 CGATCCATCTGTCCATCCATCTATTCAATTCAATTGCTGCCAAACGTATTAAATATTCAAGTCTCTCTTCTGTTGTCTAACAGATTGAGTAGGTGCATTCTAGTGGTGATCTTGTTCCTCGGATCACATACAATGCTGCATGCCAGTGCGCATTCTGCTGTAAACTGCCGTATGTCTTCTCCTCCCCTC (SEQ ID NO:374)

50

Translation:

NRLSRCIPSGDLCFPSDHIQCCNAECAFVCL (SEQ ID NO:375)

Toxin Sequence:

5 Cys-Ile-Xaa3-Ser-Gly-Asp-Leu-Cys-Phe-Xaa3-Ser-Asp-His-Ile-Gln-Cys-Cys-Asn-Ala-Xaa1-
Cys-Ala-Phe-Val-Cys-Leu-^ (SEQ ID NO:376)

10 **Name:** Cr6.5B
Species: circumcisus
Isolated: No
Cloned: Yes

15 **DNA Sequence:**

20 CGATCCATCTGTCCATCCATCTATTCAATTCAATTGCTGTCAAACGTATTAAATATT
AAGTCTCTCTTCTGTTGTCTAACAGATTGAGTTGGTGCATTCTAGTGGTGATC
TTTGTTCCTCGGATCACATACGATGCTGCAGTGCCAAGTGCAGCATTGCTCTGCTT
GTAAAAGTGCCTGATGTCTTCTCTTCCATC (SEQ ID NO:377)

Translation:

NRLSWCIPSGDLCFPSDHIRCCSAKCAFVCL (SEQ ID NO:378)

25 **Toxin Sequence:**

30 Xaa4-Cys-Ile-Xaa3-Ser-Gly-Asp-Leu-Cys-Phe-Xaa3-Ser-Asp-His-Ile-Arg-Cys-Cys-Ser-Ala-
Lys-Cys-Ala-Phe-Val-Cys-Leu-^ (SEQ ID NO:379)

35 **Name:** Cr6.6B
Species: circumcisus
Isolated: No
Cloned: Yes

DNA Sequence:

40 CGATCCATCTGTCCATCCATCTATTCAATTCAATTGCTGCCAAACGTATTAAATATT
AAGTCTCTCTTCTGTTGTCTAACAGATTGAGTAGGTGCATTCTAGTGGTGATC
TTTGTTCCTCGGATCACATACAATGCTGCAATGCCAAGTGCAGCATTGCTCTGCT
TGTAAAAGTGCCTGATGTCTTCTCTTCCATC (SEQ ID NO:380)

45 **Translation:**

NRLSRCIPSGDLCFPSDHIQCCNAKCAFACL (SEQ ID NO:381)

Toxin Sequence:

5 Cys-Ile-Xaa3-Ser-Gly-Asp-Leu-Cys-Phe-Xaa3-Ser-Asp-His-Ile-Gln-Cys-Cys-Asn-Ala-Lys-
 Cys-Ala-Phe-Ala-Cys-Leu-^ (SEQ ID NO:382)

10 **Name:** Cr6.6C
Species: circumcisus
Isolated: No
Cloned: Yes

DNA Sequence:

15 CGATCCATCTGTCCATCCATCTATTCAATTCTGCTGCCAAACTGTATTAAATATT
 AAGTCTCTCTTCTGTTGTCTAACAGATTGAGTTGGTGCATTCTAGTGGTGATC
 TTTGTTCCCGATCACATACAATGCTGCAATGCCAAGTGCACATTGCTCTGCTT
 GTAAAACGCCGTGATGTCTTACTCCCCTC (SEQ ID NO:383)

Translation:

NRLSWCIPSGDLCFPSDHIQCCNAKCAFVCL (SEQ ID NO:384)

Toxin Sequence:

25 Xaa4-Cys-Ile-Xaa3-Ser-Gly-Asp-Leu-Cys-Phe-Xaa3-Ser-Asp-His-Ile-Gln-Cys-Cys-Asn-Ala-
 Lys-Cys-Ala-Phe-Val-Cys-Leu-^ (SEQ ID NO:385)

30 -----

35 **Name:** Cr6.7
Species: circumcisus
Isolated: No
Cloned: Yes

DNA Sequence:

40 CGATCCTCTGTCTCCTCTATTATTATTCTGCTGCCAACTGTATTAAATATTCAAGTCT
 CTCTTCTGTTGTCTAACAGATTGAGTTGGTGCATTCTACTGGTGATTTGTT
 TCCCCTCGGATCACATACAATGCTGCAGTGGCAAGTGCACATTGCTGCTGATGAAA
 ACTGCCGTGATGTCTCTCCTCCCCTC (SEQ ID NO:386)

Translation:

45 NRLSWCIPTGDLCPFPSDHIQCCSGKCTFVCM (SEQ ID NO:387)

Toxin Sequence:

Xaa4-Cys-Ile-Xaa3-Thr-Gly-Asp-Leu-Cys-Phe-Xaa3-Ser-Asp-His-Ile-Gln-Cys-Cys-Ser-Gly-Lys-Cys-Thr-Phe-Val-Cys-Met-^ (SEQ ID NO:388)

5

Name: Mn6.3
Species: monachus
Isolated: No
Cloned: Yes

DNA Sequence:

15 ATGAAACTGACGTGCATGATCGTTGCTGTGCTGTTCTTGACCGCCTGGACATTGTCACGGCTGATGACTCCAGAAATGGATTGGAGAAATCTTCTCCGAAGGCACGTCA
 CGAAATGAAGAACCCCCGAAGCCTCTAAATCGAACAAAGAGATATGAGTGCTATTCTA
 CTGGTACATTTGTGGCATCAACGGAGGACTCTGCTGCAGCAACCTTGCTTATTCTA
 CGTGTGCTAACATTTCGTGTGATGTCTCTCCTCCCCCTC (SEQ ID NO:389)

20

Translation:

MKLT CMMIVAVLFLTAWTFVTADD SRNGLENLSPKARHEMKNPEASKSNKRYECYST
 GTFCG INGGLCCSNLCLFFVCLTFS (SEQ ID NO:390)

25

Toxin Sequence:

Xaa5-Xaa1-Cys-Xaa5-Ser-Thr-Gly-Thr-Phe-Cys-Gly-Ile-Asn-Gly-Gly-Leu-Cys-Cys-Ser-Asn-Leu-Cys-Leu-Phe-Phe-Val-Cys-Leu-Thr-Phe-Ser-^ (SEQ ID NO:391)

30

Name: Sm6.5
Species: stercusmuscarum
Isolated: No
Cloned: Yes

DNA Sequence:

10 ATGAAACTGACGTGCATGATCGTTGCTGTGCTGTTCTTGACCGCCTGGACATTGTCACAGCTGATGACTCCATAAATGGACCGGAGAAATAGACGAATATGGGAGAAACT
 TTTGTTGAAGGCACGTGACGAAATGAAGAACCCCCGAAGCCTCTCAATTGAGATGGT
 GCATT CCTAGTGGTGAAC TTTGTTCCGCTGGATCACATACAATGCTGCAGTGCCA
 AGTGC GCATT CGTCTGCTGTAAA ACTACCGTGATGTCTCTCCTCCATC (SEQ ID
 15 NO:392)

Translation:

MKLTCMMIVAVLFLTAWTFVTADDSINGPENRRIWEKLLLKARDEMKNPEASQLRWCI
PSGELCFRSDHIQCCSAKCAFVCL (SEQ ID NO:393)

5 **Toxin Sequence:**

Xaa4-Cys-Ile-Xaa3-Ser-Gly-Xaa1-Leu-Cys-Phe-Arg-Ser-Asp-His-Ile-Gln-Cys-Cys-Ser-Ala-Lys-Cys-Ala-Phe-Val-Cys-Leu-^ (SEQ ID NO:394)

10 -----

15 **Name:** Sm6.6
Species: stercusmuscarum
Isolated: No
Cloned: Yes

DNA Sequence:

20 ATGAAACTGACGTGTGATCGTTGCTGTGCTTCTTGATCGCCTGGACATTGTCACGGCTGATGACTCCAGAAATGGATTGAAGAATCTTTTCCGAAGGCACGTCATGAAATGAAGAACCCCGAAGCCTCTAAATTGAACAAGAGAGATGGGTGCTCTAGTGGTGGTACATTTGTGGCATCCGTCCAGGACTCTGCTGCAGCGAGTTTGCTTCTTGGTGCATAAACATTATTGATTGATGTCTTCTATTCCCCTC (SEQ ID NO:395)

25 **Translation:**

MKLTCVMIVAVLFLIAWTFVTADDSRNLKNLFPKARHEMKNPEASKLNKRDGCSSGGTFCGIRPGLCCSEFCFLWCITFID (SEQ ID NO:396)

30 **Toxin Sequence:**

Asp-Gly-Cys-Ser-Ser-Gly-Gly-Thr-Phe-Cys-Gly-Ile-Arg-Xaa3-Gly-Leu-Cys-Cys-Ser-Xaa1-Phe-Cys-Phe-Leu-Xaa4-Cys-Ile-Thr-Phe-Ile-Asp-^ (SEQ ID NO:397)

35 -----

40 **Name:** Sx6.5
Species: striolatus
Isolated: No
Cloned: Yes

DNA Sequence:

45 ATGAAACTGACGTGCATAATGACCGTTGCTGTGCTTCTTGACCGCTGGACATTGTCACGGCTGATGACTCCAGAAATGCAATTGAGAATCTTCTCTGAAGACACGTCA
CGAAGTGGAAAACCCCAAAGCCTCTAGGTGGCGGTTAGGTGCCGTCTGGTGGTA
CGGTTTGTGGCTTCCGAAACCTGGACCATACTGCTGCAGTGGCTGGTGTCTTTGT

CTGCGCCTAACCTGCCGTGATGTCTTCTCCTCCCATC (SEQ ID NO:398)

Translation:

5 MKLTCIMTVAVLFLTAWTFVTADDNRNGLENLLKTRHEVENPKASRSGGRCPGGTV
CGFPKPGPYCCSGWCFFVCA (SEQ ID NO:399)

Toxin Sequence:

10 Cys-Arg-Xaa3-Gly-Gly-Thr-Val-Cys-Gly-Phe-Xaa3-Lys-Xaa3-Gly-Xaa3-Xaa5-Cys-Cys-Ser-
Gly-Xaa4-Cys-Phe-Phe-Val-Cys-Ala-^ (SEQ ID NO:400)

15 **Name:** Sx6.6
Species: striolatus
Isolated: No
Cloned: Yes

20 **DNA Sequence:**

ATGAAACTGACGTGCGTGATGATCGTTGCTGTGCTGTTCTGACTGCCTGGACATTC
GTCACGGCTGATGACTCCAAAAATGGACTGGAGAACATTTGGAAGGCACGTGA
CGAAATGAAGAACCGCGAAGCCTCTAAATTGGACAAAAAGGAAGCCTGCTATCCGC
CTGGTACTTTTGTGGCATAAAGCCCAGGCTATGCTGCAGTGAGTTGTGTTACCGG
CCGTCTGCGTCGGTGGTTAACTGCCGTGATGTCTTCTATTCCCCTC (SEQ ID NO:401)

Translation:

30 MKLTCVMIVAVLFLTAWTFVTADDNKNGLENHFWKARDEMKNREASKLDKKEACYP
PGTFCGIKPGLCCSELCLPAVCVGG (SEQ ID NO:402)

Toxin Sequence:

35 Xaa1-Ala-Cys-Xaa5-Xaa3-Xaa3-Gly-Thr-Phe-Cys-Gly-Ile-Lys-Xaa3-Gly-Leu-Cys-Cys-Ser-
Xaa1-Leu-Cys-Leu-Xaa3-Ala-Val-Cys-Val-Gly-# (SEQ ID NO:403)

40 **Name:** Sx6.7
Species: striolatus
Isolated: No
Cloned: Yes

45 **DNA Sequence:**

ATGAAACTGACGTGCTGATGGCTGTTGCTGTGCTGTTCTGACCGCCGGACATTC

5 GTCACGGCTGATGACTCCAGAAATGGATTGGAGAATCTTCTCCGAAGGCACGTCA
 CGAAATGAAGAACCCCGAAGCCTCTAAATCGAACAAAGAGATATGAGTGCATTCTA
 CTGGTACATTGTGGCATCAACGGAGGACTCTGCTGCAGCAACCTTGCTTATTCTA
 CGTGTGCTAACATTTCGTATGGCTTCTATCCCCTC (SEQ ID NO:404)

10 **Translation:**

MKLTCMAVAVLFLTARTFVTADDNRNGLENLSPKARHEMKNPEASKSNKRYECYST
 GTFCGNGGLCCSNLCLFFVCLTFS (SEQ ID NO:405)

15 **Toxin Sequence:**

Xaa5-Xaa1-Cys-Xaa5-Ser-Thr-Gly-Thr-Phe-Cys-Gly-Ile-Asn-Gly-Gly-Leu-Cys-Cys-Ser-Asn-
 Leu-Cys-Leu-Phe-Phe-Val-Cys-Leu-Thr-Phe-Ser-^ (SEQ ID NO:406)

20 **Name:** Sx6.8
Species: striolatus
Isolated: No
Cloned: Yes

25 **DNA Sequence:**

ATGAAACTGACGTGTATGGTATCGTCGCCGTGCTGCTCCTGACGACCTGTCATCTC
 ATCACAGCTGATGACTCCAGAGGTACGCAGAACATCGTCCCTGAGGTCGACTAC
 CAAAGTCTCCAAGTCGACTAGCTGCATGAAAGCCGGGTCTTATTGCGTCGCTACTAC
 GAGAATCTGCTGCGTTATTGCGCTTATTGGCTATCCAA
 AAACTGATCCTCCCCCTACTGTGCTCTACCTTCTGCCTGATGTCTTCCTCCCC
 30 TC (SEQ ID NO:407)

35 **Translation:**

MKLTCMVIVAVLLLTTCHLITADDRGQTQKHRSLRSTTKVSKSTSCMKAGSYCVATTRI
 CCGYCAYFGKICIGYPKN (SEQ ID NO:408)

40 **Toxin Sequence:**

Ser-Thr-Ser-Cys-Met-Lys-Ala-Gly-Ser-Xaa5-Cys-Val-Ala-Thr-Thr-Arg-Ile-Cys-Cys-Gly-Xaa5-
 Cys-Ala-Xaa5-Phe-Gly-Lys-Ile-Cys-Ile-Gly-Xaa5-Xaa3-Lys-Asn-^ (SEQ ID NO:409)

45 Xaa1 is Glu or γ -carboxy-Glu

Xaa2 is Gln or pyro-Glu

Xaa3 is Pro or hydroxy-Pro

Xaa4 is Trp or bromo-Trp

Xaa5 is Tyr, 125 I-Tyr, mono-iodo-Tyr, di-iodo-Tyr, O-sulpho-Tyr or O-phospho-Tyr

Xaa6 is Nle

' is free carboxyl or amidated C-terminus, preferably free carboxyl

is free carboxyl or amidated C-terminus, preferably amidated

TABLE 2

Alignment of Conotoxin Peptide Sequences

10	δ-GmVIA [F15Y] δ-GmVIA [F27Y] Gmaria9 Tau..11 Tau..16 Tau..18 Tau..19 δ-TkVIA [M8J]	-VKPCPKESQLCDPIYQN--CCF GWNC--VLF-CV^ (SEQ ID NO: 4) -VKPCPKESQLCDPIFQN--CCF GWNC--VLY-CV^ (SEQ ID NO: 5) M---CFHEAQQLCDPIEQN--CCH GLFC--VLV-CV^ (SEQ ID NO: 2) QVKPCPKEHQLCLILIFQN--CCF GWYC--VVLSCCT^ (SEQ ID NO: 11) ----CVPHESPCNWLTQN--CCF GYNC--IIFFCLT^ (SEQ ID NO: 14) QVKPCPKEHQLCLILIFQN--CCF GWYC--LLRPCLT^ (SEQ ID NO: 17) -VKPCSRERQLCDPLSQN--CCF GWHC--VLVSCV^ (SEQ ID NO: 2) W---CERSEPKCMLLDQN--CCL GY-C--VVLVCT^ (SEQ ID NO: 14) ----CL RYGEVCDIFFFCI--CC- GY-C--VLLFCCT^ (SEQ ID NO: 37) ----CERL RYSCDVISQN--CCG ST-C--VFF-CL^ (SEQ ID NO: 40) ----CFLAL RSCMVFSLQN--CCT GL-C--LGF-CV^ (SEQ ID NO: 43) ----CVERYR GECNWLTQN--CCI EL-C--VFF-CL^ (SEQ ID NO: 16) ----CFLAL RBCVLFVSIR--CCT GL-C--LGF-CTW^ (SEQ ID NO: 42) ----CIA RYEVCIIFFFCI--CC- GY-C--VLLFCAT^ (SEQ ID NO: 51) ----CIAEHETCNIFTQN--CCF GV-C--IFI-CV^ (SEQ ID NO: 57) ----CII HFDCPPIRHT--CCF GL-C--LLIACI^ (SEQ ID NO: 60) ----CII F RACIILYLN--CC- GY-C--VGAICL^ (SEQ ID NO: 61) ----CIAHHELCNIFIQN--CCI GT-C--LLI-CL^ (SEQ ID NO: 66) ----CII FELCIIFFFCI--CC- GY-C--VLLVCL^ (SEQ ID NO: 62) ----CIAI FELCI ALDN--CCS GV-C--MVFFCL^ (SEQ ID NO: 63) ----CII F RACIILYLN--CC- GY-C--VGAVCL^ (SEQ ID NO: 64) ----CIVYI LDPCVMLRH--CCF GL-C--VLIACI^ (SEQ ID NO: 65) ----CII F RVCNCFFFPN--CC- GY-C--VALVCL^ (SEQ ID NO: 66) ----CII 2PDPCTMVRHT--CCF GL-C--VLIACSHTA^ (SEQ ID NO: 84) ----CRAE RACMIIITQN--CCL GY-C--LFF-CL^ (SEQ ID NO: 67) ----CII F RBCI IFFPN--CCS GW-C--VLLVCA^ (SEQ ID NO: 68) ----CII F RBCI ILLFPS--CCS GW-C--EVLVCA^ (SEQ ID NO: 69) ----CII F RVCNCFFFPN--CC- GY-C--VLLVCL^ (SEQ ID NO: 70) ----CII F RVCNCFFFPN--CC- GY-C--VLLLCI^ (SEQ ID NO: 71) ----CQAE RVCNCFFFPN--CC- GY-C--VLLLCI^ (SEQ ID NO: 72) ----CII HFDCPPIRHT--CCF GL-C--LLIACI^ (SEQ ID NO: 102) ----CII F RVCNCFFFPN--CC- GY-C--VLLVCL^ (SEQ ID NO: 103) SKKQCF, N RVCI ANLAH--CC, GPC-C--FLF-CLNQ^ (SEQ ID NO: 108) ----CII, S RVCIVILED--CCNIF-C--IIFFCI^ (SEQ ID NO: 111) ----CII F RBCI IFFPN--CCN GY-C--VQFICL^ (SEQ ID NO: 114) ----CII A RMCQI LFNEK--CC, GW-C--IILFCA^ (SEQ ID NO: 117) ----CII C RBCI ILLFES--CC, GW-C--IVLVCA^ (SEQ ID NO: 120) ----CII F RLCQVVEIN--CC, GY-C--FIVVCFI^ (SEQ ID NO: 123) -DDECEPPI RDCI IFFFI GP-PCC, GW-C--FLW-CA^ (SEQ ID NO: 126) -IDDECEPPI RDCI IFFFI GP-PCC, GW-C--FLW-CA^ (SEQ ID NO: 127) -IDDECEPPI RNFCA MIKI GP-PCC, GW-C--FFA-CA^ (SEQ ID NO: 128) -IDDECEPPI RNFCA MIKI GP-PCC, GW-C--FFA-CA^ (SEQ ID NO: 129) -IDDECEPPI RNFCA MIKI GP-PCC, GW-C--FFA-CA^ (SEQ ID NO: 138) -ID--CII F RNFCA WPII GP-LCC, GW-C--LYV-CN^ (SEQ ID NO: 141) -CII DCLWKKNC RFPKIGG-PCC, GL-C--FFV-CA^ (SEQ ID NO: 144) D--CII R RPFCA LPQLGL-LCCS R-C--LLF-CV^ (SEQ ID NO: 147) -IG-CII R RPFCA LPQLGL-LCCS R-C--LLF-CV^ (SEQ ID NO: 150) -FA-CII R STAC S---IKOGLCC, R F-C--LPGVCFG^ (SEQ ID NO: 154) -FA-CII R STAC S---IKOGLCC, R F-C--LPGVCFG^ (SEQ ID NO: 155) -FA-CII R STAC S---IKOGLCC, R F-C--LPGVCFG^ (SEQ ID NO: 156) -IG-CII AGTFCG---IRPGLCC, R F-C--FLW-CITFV^ (SEQ ID NO: 159) -DE-CYPPGTFCG---IKPGLCC, R F-C--LSFVCISF-DF^ (SEQ ID NO: 162)
15	Tau..4 Tau..15 Tau..16 Tau..18 Tau..19 Tau..20	
20	Tau..21 Tau..22 Tau..23 Tau..24 Tau..25 Tau..26 Tau..27 Tau..28 Tau..29 Tau..30	
25	Tau..31 Tau..32 Tau..33 Tau..34 Tau..35 Tau..36 Tau..37 Tau..38 Tau..39 Tau..40	
30	Tau..41 Tau..42 Tau..43 Tau..44 Tau..45 Tau..46 Tau..47 Tau..48 Tau..49 Tau..50	
35	Tau..51 Tau..52 Tau..53 Tau..54 Tau..55 Tau..56 Tau..57 Tau..58 Tau..59 Tau..60	
40	Tau..61 Tau..62 Tau..63 Tau..64 Tau..65 Tau..66 Tau..67 Tau..68 Tau..69 Tau..70	
45	Tau..71 Tau..72 Tau..73 Tau..74 Tau..75 Tau..76 Tau..77 Tau..78 Tau..79 Tau..80	
50	Tau..81 Tau..82 Tau..83 Tau..84 Tau..85 Tau..86 Tau..87 Tau..88 Tau..89 Tau..90	
55	Tau..91 Tau..92 Tau..93 Tau..94 Tau..95 Tau..96 Tau..97 Tau..98 Tau..99 Tau..100	

M6.7
 M6.8
 E6.4
 F6.4
 5 8-SVIE [D1E]
 8-SVIE
 G6.1
 G6.2
 G6.3
 G6.7
 10 F6.1
 F6.2
 G6.1
 G6.1
 F6.6
 15 F6.6
 A6.10
 T6.10
 G6.4
 G6.5
 20 F6.5
 I6.7
 F6.5
 F6.5
 F6.5
 F6.5
 25 F6.10
 F6.14
 G6.14
 G6.14
 G6.14
 30 F6.6
 F6.7
 F6.8
 F6.5
 F6.2
 35 triat21
 SS-riatus 26
 AS-riatus 106
 .7
 F6.9
 40 A6.1 (F763)
 A6.11 (G21)
 A6.12 (G20)
 A6.5 (F108)
 A6.5 (G211)
 45 S6.1 (J415)
 S6.2 (J414)
 S6.3
 S6.1 (G18)
 F6.6 (F076)
 50 S6.1 (A607)
 S6.1 (F775)
 M6.2 (G218)
 M6.4 (A666)
 F6.3 (F770)
 55 S6.1
 S6.2 (F024)
 S6.3 (F026)
 T6.2 (F078)
 T6.4 (F080)
 60 T6.8
 A6.1

-EA-CYNAGGFCG---IHI NLCCSEF-C--ILW-CITFVLS# (SEQ ID NO:165)
 -EA-CYNAJTFCG---IHI NLCCSAI-C--LSFVCISF-LF# (SEQ ID NO:168)
 -EA-CYPEJTFCG---IHF NLCCSEL-C--LPAVCVG# (SEQ ID NO:171)
 -EA-CYPEJTFCG---IHF NLCCSEL-C--LPAVCVG# (SEQ ID NO:174)
 -E 6-CNSG JTFCG---IHF NLCCSEF-C--FLW-CITFII (SEQ ID NO:177)
 -D 6-CNSG JTFCG---IHF NLCCSEF-C--FLW-CITFII (SEQ ID NO:180)
 -Y 6-CNSA WAFCG---IHF NLCCSEL-C--LWV-CT# (SEQ ID NO:184)
 -Y 6-CNSA WAFCG---IHF NLCCSEL-C--LGW-CT# (SEQ ID NO:187)
 -YE-CYLINHFCG---IHF NLCCCSNL-C--LFFFCLTFS# (SEQ ID NO:190)
 -D 6-CIPEJTFICA---FUMRLCCS6K-C--MLV-CL# (SEQ ID NO:193)
 -II-CFPEJTFMFCG---VHF VLCCS6N-C--LLI-CV# (SEQ ID NO:196)
 ---CYD6GJTGCD---S6NQCCSGW-C--IFV-CL# (SEQ ID NO:199)
 ---CYD6GJTGCD---S6NQCCSGW-C--IFV-CL# (SEQ ID NO:200)
 ---CFESWVACE---S6P6CCSHV-C--LFV-CT# (SEQ ID NO:201)
 ---CNEA2EHC7---QHF DCCSES-CNKFVGFCLN# (SEQ ID NO:205)
 ---CYI GFTSCN---T V6NCCS 6W-C--LFV-CL# (SEQ ID NO:211)
 ---CY5GFTSCN---T V6NCCS 6W-C--LFV-CL# (SEQ ID NO:214)
 -D 6-CORI1WVCPVPLLN6 V6CCV 6LIC--GPFVFCIGW# (SEQ ID NO:217)
 KT---CQHFWDFCPGSLV 6V1TCCG6LIC--FLFFCV# (SEQ ID NO:218)
 -I 6-CQHFWDVCPVPLW V6YCCD6FIC--PSFFCA# (SEQ ID NO:219)
 -I 6-CQHFWDVCPVPLW V6YCCD6FIC--GPFVCV# (SEQ ID NO:226)
 -G 6-CLENVYFCGIPFVNN6LCCS 6N-C--VFV-C--EP# (SEQ ID NO:229)
 ---CINWVYFCGIPFVNN6LCCS 6N-C--VFV-C--EP# (SEQ ID NO:232)
 -F 6-CLEANVYCYL6FV 6N V6CCS 6N-C--VFV-CIAQF FRK# (SEQ ID NO:235)
 -I 6-CLE6VYFCGIPFVNN6LCCS 6N-C--VFV-CIAQF FRK# (SEQ ID NO:238)
 -A 6-CSRFWEYCFVPLIL 6V6YCC6LIC--GPFVCV# (SEQ ID NO:244)
 -L 6-CLMVYFCGIPFVNN6LCCS 6N-C--VFV--CLH6FENP# (SEQ ID NO:245)
 ---CLV6FPC6WLTIA V6ECC6H6K-C--FMM-CW# (SEQ ID NO:250)
 -I 6-CHMVYFCGIPFVNN6LCCS 6N-C--LGW-CA# (SEQ ID NO:250)
 -P 6-CTAN6FRCRISV6FV6LCCS 6R-C--VFV-CI# (SEQ ID NO:251)
 -F 6-CTAN6FRCRISV6FV6LCCS 6R-C--VFV-CI# (SEQ ID NO:251)
 -R 6-CRPFV6FCG6FV6LCCS 6R-C--IFV-CV# (SEQ ID NO:251)
 -U 6-CIP 6WFC6F6N 6I 6V6LCCS 6T-C--LVV-CM# (SEQ ID NO:262)
 -D 6-CIP 6ENC--DV6FV6YRC6C 6T-C--I6V6CA# (SEQ ID NO:266)
 -L 6RW6CIP 6ELC--F6S6H6C6C 6H-C--AFV-CL# (SEQ ID NO:268)
 ---WCIP 6ELC--F6S6H6C6C 6H-C--AFV-CL# (SEQ ID NO:270)
 ---WCIP 6ELC--F6S6H6C6C 6H-C--AFV-CL# (SEQ ID NO:271)
 -L 6RW6CIP 6FVC--R6T6FV6CC6H-C--F6V-C# (SEQ ID NO:272)
 ---CLP 6TSC---L6F6F6C6C--I6T-C6S6L6SC6V# (SEQ ID NO:273)
 ---C6F6F6FCG6F6H 6T-C6N6W-CF--F6V-CI# (SEQ ID NO:273)
 ---CLE6V6L6C6--F6A6W-C6C6E-CV--I6V-CI# (SEQ ID NO:274)
 -E 6-CVA 6F6C6F6H 6T-C6N6W-CF--F6V-CI# (SEQ ID NO:274)
 -D 6-CF6V6YFCGIPFV6WRC6C6L-C6--I6V-CV# (SEQ ID NO:284)
 ---C6V6F6FCG6--F6G6W-C6C6F6-C6-CI# (SEQ ID NO:284)
 ---C6V6F6FCG6--F6G6W-C6C6F6-C6-CI# (SEQ ID NO:284)
 ---C6V6F6FCG6--F6G6W-C6C6F6-C6-CI# (SEQ ID NO:284)
 ---C6V6F6FCG6--F6G6W-C6C6F6-C6-CI# (SEQ ID NO:284)
 -G 6-CL6V6FCGIPFV6LCC6N-CV--F6V-C6I# (SEQ ID NO:283)
 Q 6-CF6V6F6C6M6--F6A6W-C6C6F6-CF--F6V-CM# (SEQ ID NO:285)
 -A 6-C6V6F6C6M6--F6A6W-C6C6F6-CF--F6V-CI# (SEQ ID NO:285)
 ---C6V6F6L6C6D6--F6P6YCC6W-C6-CI# (SEQ ID NO:285)
 -E 6-GBC6T6F6C6F6K6--I6P6C6W-CF--F6V-CI# (SEQ ID NO:291)
 -E 6-C6V6F6C6F6K6--I6P6C6W-CF--F6V-CI# (SEQ ID NO:291)
 -D 6-CW6V6YWF6C6L6Q6---CCP 6T6CF--F6L-CF# (SEQ ID NO:293)
 ---WC6V6F6L6C6I6P6V# (SEQ ID NO:296)
 ---CYI 6TSC---N6P6-CC6S6W-CI--F6V-CI# (SEQ ID NO:296)
 W 6-CIPRGD6L6--F6S6L6I6Q6-CC6S6K6-CTF--V6C6I# (SEQ ID NO:296)

5 Ac6.2 -G--CVPSGEIC-YFMDHIG-CCSGK-CTF---VCM^ (SEQ ID NO: 349)
 Bu6.7 -DE-CSAPGAFCL--IFPGL-CCSEF-C-FF--ACF^ (SEQ ID NO: 352)
 Bu6.8 -C--CLPRWEFC-PIFFKND-CCSGI-CIS---ICL^ (SEQ ID NO: 355)
 Cn6.10 -DG-CYNAGTFCG--IFPGL-CCSEF-C-FL--WCITFVDS# (SEQ ID NO: 364)
 Cn6.1 -YE-CYSTGTFCG--IMGGL-CCSNL-CLFF--VCLTFS^ (SEQ ID NO: 361)
 Cr6.5 W---CIPSGELC-FPSDHIQ-CCSAK-CAF---VCL^ (SEQ ID NO: 370)
 Cr6.5A ----CIPSGELC-FPSDHIQ-CCSAK-CAF---VCL^ (SEQ ID NO: 373)
 Cr6.6 ----CIPSGELC-FPSDHIQ-CCNAK-CAF---VCL^ (SEQ ID NO: 367)
 Cr6.6A ----CIPSGELC-FPSDHIQ-CCNAE-CAF---VCL^ (SEQ ID NO: 371)
 10 Cr6.6B W---CIPSGELC-FPSDHIQ-CCSAK-CAF---VCL^ (SEQ ID NO: 374)
 Cr6.6B ----CIPSGELC-FPSDHIQ-CCNAK-CAF---ACL^ (SEQ ID NO: 381)
 Cr6.6C W---CIPSGELC-FPSDHIQ-CCNAK-CAF---VCL^ (SEQ ID NO: 385)
 Cr6.7 W---CIPSGELC-FPSDHIQ-CCSGK-CTF---VCM^ (SEQ ID NO: 384)
 Mn6.3 -YE-CYSTGTFCG--IMGGL-CCSNL-CLFF--VCLTFS^ (SEQ ID NO: 391)
 15 Sm6.5 W---CIPSGELC-FPSDHIQ-CCSAK-CAF---VCL^ (SEQ ID NO: 394)
 Sm6.6 -DG-CSEGSTFCG--IFPGL-CCSEF-C-FL--WCITFID^ (SEQ ID NO: 397)
 Sx6.4 -D--CLARKDAFCAWPILGPL-CCSRL-CLY---VCM^ (SEQ ID NO: 395)
 Sx6.5 ----CKFGSTVCGFPKIGPY-CCS3W-CFF---VCA^ (SEQ ID NO: 404)
 Sx6.6 -EA-CYEPGTFCG--IFPGL-CCSRL-CLPA--VCVG# (SEQ ID NO: 403)
 20 Sx6.7 -YE-CYSTGTFCG--IMGGL-CCSNL-CLFF--VCLTFS^ (SEQ ID NO: 406)
 Sx6.8 STS-CMKAGSYCVATTN--I-CC-3Y-CAYFGKICISYPKN^ (SEQ ID NO: 409)

X is Nle

25 It will be appreciated that the methods and compositions of the instant invention can be incorporated in the form of a variety of embodiments, only a few of which are disclosed herein. It will be apparent to the artisan that other embodiments exist and do not depart from the spirit of the invention. Thus, the described embodiments are illustrative and should not be construed as restrictive.

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LIST OF REFERENCES

Barnay, G. et al. (2000). *J. Med. Chem.*
 Bitan, G. et al. (1997). *J. Peptide Res.* **49**:421-426.
 Bodansky et al. (1966). *Chem. Ind.* **38**:1597-98.
 35 Cartier, G.E. et al. (1996). *J. Biol. Chem.* **271**:7522-7528.
 Cornell-Bell, A.H. et al. (1999). Kainate spiral waves and integrins: A signaling system without gap junctions. *Glia*, in press.
 Craik, D.J. et al. (2001). *Toxicon* **39**:43-60.
 Cruz, L.J. et al. (1976). *Verliger* **18**:302-308.
 40 Ettinger, L.J. et al. (1978). *Cancer* **41**:1270-1273.
 Fainzilber, M. et al. (1991). *Eur. J. Biochem.* **202**:589-595.
 Fainzilber, M. et al. (1995). *J. Biol. Chem.* **270**:1123-1129.
 Hammerland et al. (1992). *Eur. J. Pharmacol.* **226**:239-244.
 Hillyard, D.R. et al. (1989). *Biochemistry* **28**:358-361.

Horiki, K. et al. (1978). *Chemistry Letters* 165-68.

Hubry, V. et al. (1994). *Reactive Polymers* **22**:231-241.

Kapoor (1970). *J. Pharm. Sci.* **59**:1-27.

Kornreich, W.D. et al. (1986). U.S. Patent No. 4,569,967.

5 Luer, M.S. & Hatton, J. (1993). *Annals Pharmacotherapy* **27**:912-921.

Martinez, J.S. et al. (1995). *Biochem.* **34**:14519-14526.

McIntosh, J.M. et al. (1982). *Arch. Biochem. Biophys.* **218**:329-334.

McIntosh, J. M. et al. (1998). *Methods Enzymol.* **294**:605-624.

10 *Methoden der Organischen Chemie (Houben-Weyl): Synthese von Peptiden*, E. Wunsch (Ed.), Georg Thieme Verlag, Stuttgart, Ger. (1974).

Myers, R.A. et al. (1991). *Biochemistry* **30**:9370-9377.

Nakamura, T. et al. (1996). *Protein Sci.* **5**:524-530.

Nishiuchi, Y. et al. (1993). Synthesis of gamma-carboxyglutamic acid-containing peptides by the Boc strategy. *Int. J. Pept. Protein Res.* **42**:533-538.

15 Nowak, L. et al. (1984). *Nature* **307**:462-465.

Olivera, B.M. et al. (1984). U.S. Patent 4,447,356.

Olivera, B.M. et al. (1985). *Science* **230**:1338-1343.

Olivera, B.M. et al. (1990). *Science* **249**:257-263.

Olivera, B.M. et al. (1996). U.S. Patent 5,514,774.

20 Ornstein, et al. (1993). *Biorganic Medicinal Chemistry Letters* **3**:43-48.

Plone, M. A. et al. (1996). *Pain* **66**:265-70.

Plummer, J. L. et al. (1991). *J Pharmacol Methods* **26**:79-87.

Rivier, J.R. et al. (1978). *Biopolymers* **17**:1927-38.

Rivier, J.R. et al. (1987). *Biochem.* **26**:8508-8512.

25 Sambrook, J. et al. (1989). *Molecular Cloning: A Laboratory Manual*, 2nd Ed., Cold Spring Harbor Laboratory, Cold Spring Harbor, NY.

Schroder & Lubke (1965). *The Peptides* **1**:72-75, Academic Press, NY.

Shon, K.-J. et al. (1994). *Biochemistry* **33**:11420-11425.

Stewart and Young, *Solid-Phase Peptide Synthesis*, Freeman & Co., San Francisco, CA (1969).

30 Suh, H.H. et al. (1992). *Eur J Pharmacol* **213**:337-41.

Vale et al. (1978). U.S. Patent 4,105,603.

Van de Steen, P. et al. (1998). *Critical Rev. in Biochem. and Mol. Biol.* **33**:151-208.

Woolfe, G. and MacDonald, A. (1944). *J. Pharmacol. Exp. Ther.* **80**:300-307.

Zafaralla, G.C. et al. (1988). *Biochemistry* **27**:7102-7105.

Zhou L.M., et al. (1996). *J. Neurochem.* **66**:620-628.

Zimm, S. et al. (1984). *Cancer Res.* **44**:1698-1701.

U.S. Patent No. 3,972,859.

U.S. Patent No. 3,842,067.

5 U.S. Patent No. 3,862,925.

U.S. Patent No. 5,514,774.

U.S. Patent No. 5,531,001.

U.S. Patent No. 5,534,615.

U.S. Patent No. 5,364,769.

10 U.S. Patent No. 5,545,723.

U.S. Patent No. 5,550,050.

U.S. Patent No. 5,591,821.

U.S. Patent No. 5,719,264.

U.S. Patent No. 5,844,077.

15 PCT Published Application WO 92/19195.

PCT Published Application WO 94/25503.

PCT Published Application WO 95/01203.

PCT Published Application WO 95/05452.

PCT Published Application WO 96/02286.

20 PCT Published Application WO 96/02646.

PCT Published Application WO 96/11698.

PCT Published Application WO 96/40871.

PCT Published Application WO 96/40959.

PCT Published Application WO 97/12635.

25 PCT Published Application WO 98/03189.

PCT Published Application WO 00/23092.